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GASTRIC ULCER*

A Study of the Massachusetts General Hospital Cases During the Ten-Year Period 1938-1947

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GASTRIC ulcer has been recognized as a clinical entity for many years. However, it is so closely related to duodenal ulcer on the one hand and gastric cancer on the other that various authorities tend to emphasize either the benign or the malignant aspect to the exclusion of the other. Obviously, in the former case, gastric ulcer would become a minor subdivision of peptic ulcer, and the surgical treatment would consist of control of the complications. In the latter, gastric ulcers are regarded as actually malignant, or so similar to gastric cancer that all should be operated on and the only remaining problems are technical details involved in gastric resection.

Therefore it has seemed important to re-examine the management of patients with gastric ulcer on the basis of the cases studied in the Massachusetts General Hospital during the ten-year period 1938-1947. Additional knowledge of several aspects of the problem has been gained during this time. The most important include a study of the ulcer-cancer relation, the treatment of the most common complication of gastric ulcer (hemorrhage) and the development of a satisfactory operative technic, especially for ulcers about the cardia.

General Considerations

The diagnosis of gastric ulcer was made in a total of 512 patients in this period (Table 1). Acute perforations have been excluded, since later study has proved that many of them actually are due to duodenal rather than gastric ulcer. The average age at admission to the hospital was fifty-five years, the distribution according to age groups being as follows: ten to nineteen, 0.6 per cent; twenty to twenty-nine, 2.8 per cent; thirty to thirty-nine, 8.4 per cent; forty to forty-nine, 20.4 per cent; fifty to fifty-nine, 32.4 per cent; sixty to sixty-nine, 22.8 per cent; seventy to seventy-nine, 12.2 per cent; and eighty to eighty-nine, 0.4 per cent. About an eighth of the patients appeared before forty years of age, and an eighth after seventy. Since the duration of symptoms before admission averaged approximately five years, the average age at onset was fifty. Gastric ulcer therefore is essentially a disease of the older age groups, in contrast to duodenal ulcer, in which the average age at onset of symptoms is about thirty.

TABLE 1. *Distribution of Cases of Gastric Ulcer.*

TREATMENT	1938–1942	1943–1947	TOTALS
Medical	113	104	217
Surgical	104	191	295
Totals	217	295	512
Percentage of operations	48	65	58

The disease is almost exactly three times as common in males (74 per cent) as it is in females (26 per cent).

Problem of Ulcer and Cancer

Early studies by Holmes and Hampton[1] indicated that all prepyloric ulcerations were malignant, and Sproull[2] proved the extreme rarity of benign ulcer on the greater curvature. In recent years, improved x-ray technics and the use of the gastroscope have demonstrated many ulcers that would have been overlooked twenty years ago. Coincidentally, there has been a great increase in the number of gastric resection so that histologic confirmation of the clinical diagnosis has been possible much more frequently than it was heretofore.

It is clear that the greater the number of resections the more accurate will be the estimated error in the diagnosis of cancer. For in some cases treated medically as benign ulcer the patients will certainly die of cancer of the stomach, but only rarely can these patients be followed long or closely

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enough for a final diagnosis to be made. Consequently, the cases reported below, in which an aggressive surgical attack has led to resections in nearly 60 per cent of the entire series, are especially significant.

In this group, 34 of the 512 cases originally diagnosed as gastric ulcer were finally found to be cancer. This was an over-all diagnostic error of 6.6 per cent. Of the patients who had resections and therefore final diagnoses, 32 out of 295, or 10.8 per cent, were proved to have cancer (Table 2).

TABLE 2. *Error in Diagnosis of Cancer.*

GROUP	ORIGINAL DIAGNOSIS OF BENIGN ULCER	FINAL DIAGNOSIS OF CANCER	ERROR IN DIAGNOSIS
			%
All cases	512	34	6.6
Cases with resections	295	32	10.8

The absolute diagnostic error therefore now lies between 6.6 and 10.8 per cent, and we believe that it is very near to 10 per cent. Since the error in a previous study was at least 14 per cent,[3] there has been definite improvement during the past decade. It is pertinent to inquire why this change has occurred and to discuss briefly the differential diagnosis of benign ulcer and cancer.

In the first place, it is well to emphasize that the clinician is almost wholly at the mercy of the radiologist and gastroscopist so far as diagnosis is concerned. To illustrate this point, it may be noted as shown previously[3] that 65 per cent of the lesions in the prepyloric area that demonstrate ulceration are cancer. But, at present, with the use of spot films, when a highly competent radiologist calls an ulcer in this area benign, his diagnostic error will be approximately 10 per cent.

No one appreciates his limitations in this respect more than the radiologist, who realizes his inability to make a microscopical diagnosis. It has therefore become the custom to report this group of ulcers as "gastric ulcer, grossly benign." The gastroscopist is limited in the same fashion. To their interpretations, data of less diagnostic importance may be added, including the duration of symptoms, the location of the lesion, the size of the ulcer, the gastric analysis, the cytologic smear of the gastric contents, the presence or absence of accompanying ulcers or complications, and the rate of healing under medical therapy to help distinguish ulcers that are microscopically benign from ulcers that are microscopically malignant ("ulcer-cancer").

AGE AND DURATION OF SYMPTOMS

A short gastric history in a patient fifty years of age or over is highly suggestive of cancer. The average duration of symptoms in patients with "ulcer-cancer" before entry to the hospital is one and a half years, compared with a duration of five years in patients with benign ulcers. The duration of symptoms with "ulcer-cancer" varied from less than a month to ten years. The ages varied from twenty-six to seventy-seven years for ulcer-cancer, whereas the average age of the entire group was fifty-one years.

LOCATION OF THE LESION

Increasing accuracy in x-ray technic has resulted in the differentiation of many of the benign ulcers and ulcerating carcinomas, especially in the prepyloric area. At present the diagnosis of benign ulcer in the pyloric and prepyloric areas is nearly as accurate as and the error in diagnosis of cancer not much higher than that of lesions on the mid-lesser curvature. Schatzki and Eyler[4] have found, in an independent review of the same cases, that the radiologic diagnostic error of gastric lesions throughout the stomach is highest in the region of the cardia, less in the prepyloric area and least along the mid-lesser curvature. It is of interest to note that in the period from 1938 to 1947, 6 benign ulcers of the greater curvature were resected.

SIZE OF THE ULCER

Although previous studies have shown that the incidence of cancer increases with the size of the ulceration, very little attention should be paid to this feature in the individual case. It is apparent that early operation will increase the number of resected small ulcerating carcinomas. In this series, the average diameter of the malignant ulcer was 1.8 cm., and only 1 was over 2.5 cm. The benign ulcers that were resected averaged 1.6 cm., and the largest benign ulcer was 7.0 cm. in diameter.

GASTRIC ANALYSIS

The presence of free hydrochloric acid is of no significance although its absence after the use of histamine is strongly suggestive of cancer. Free hydrochloric acid is found in approximately 90 per cent of the patients with benign ulcer and of those with ulcer-cancer. About 40 per cent of carcinomas of the stomach are accompanied by histamine achlorhydria.

CYTOLOGIC SMEAR

A positive Papanicolaou[5] smear of the gastric sediment demonstrating cancer cells is of immense importance if the interpretation is made by a competent technician. If the smear is positive, the lesion is almost sure to be cancer, since Graham et al.[6] found only 4 per cent false-positive tests. If the smear is negative, cancer may still be present since approximately a third of the carcinomas of the stomach fail to show cells when usual methods are employed. Careful preparation of specimens diminishes this error,[6] and it is possible that further experience with such substances as

eugenol will increase the accuracy of this test even more.

The presence of an accompanying active duodenal ulcer is strong evidence that the gastric ulcer is benign. Figures from the Mayo Clinic[7, 8] indicate that 0.1 per cent of patients with duodenal ulcer will have carcinoma of the stomach, and 1 per cent of those with duodenal ulcer will have an associated benign ulcer of the stomach.

The presence of multiple gastric ulcers also suggests that the lesions are benign. However, all combinations of ulcer and cancer are seen occasionally, with multiple benign ulcers, associated benign duodenal or gastric ulcer and distinct carcinoma, and multiple ulcerating carcinomas.

In this series multiple gastric ulcers were found in 8 per cent of the patients. Four distinct ulcers were present in one case. Four per cent of the patients had associated gastric and duodenal ulcers.

Complications of Gastric Ulceration

Incidence

Massive hemorrhage appears to be slightly less frequent with malignant ulcers than with benign since it occurred in only 6 per cent of the cases of ulcer-cancer, compared with benign ulcer, in which the incidence was 9 per cent. On the other hand, pyloric obstruction was much more common, occurring in 19 per cent of the ulcer-cancer group, and in only 1.2 per cent of the benign cases. Perforations, nearly always walled off by adjacent viscera, occur with about equal frequency in both groups.

Rate of Healing

The rate of healing of a gastric ulcer is still regarded as the most reliable differential feature between benign ulcer and cancer. Even this fact is not absolute, since in this series two ulcers apparently healed entirely under hospital care but recurred shortly thereafter, and resection proved them to be carcinoma. These rare cases, however, are exceptions to the rule that only benign ulcers tend to heal rapidly. It is also true that some ulcers that prove to be benign fail to heal in a period of months, especially in the older age groups.

This method of differentiation has been applied in a large number of cases in this hospital. In patients that have done well under medical management, significant improvement is usually apparent after a three-week interval. Although complete healing is rare at this time, it occasionally occurs. The average ulcer has healed completely in two months, although at times as long a period as four months is required before the lesion entirely disappears. Consequently, the decision to abandon or continue medical treatment must usually be made a month after the patient is admitted to the hospital. In individual cases, especially in older patients, it may be necessary to wait longer for healing. Such patients must be followed closely, however, until healing is complete.

The proponents of immediate operation for all gastric ulcers[9] maintain that this delay is very dangerous from the point of view of spread of misdiagnosed cancers during the interval. On the other hand, it may be pointed out that since the average duration of symptoms before the patient arrives in the hospital is one and a half years, the relatively short extra delay should impose little hazard.

This point obviously cannot be proved by statistics. But it is of interest that of the patients who were believed to have benign ulcer but who were operated on with a delay of less than one month after reaching the hospital, 40 per cent are living and well five years later; of those who were followed for six months or more and then were found to have cancer at operation, all are dead of the disease.

In summary, it is certain that the differential diagnosis of ulcer and cancer cannot be made by present technics in about 10 per cent of the cases. From the point of view of cancer control all gastric ulcers should therefore be operated on at once. However, with care, it is possible to select a small group that can be managed medically if they are closely followed. Following these principles, 97 per cent of the patients who had resections for gastric ulcer were treated correctly. It is of interest that the 9 patients in this series who were followed an inordinate period before resection (the errors in judgment) were exactly equal in number to the deaths after resection.

Types

The complications of gastric ulcer are the same as those of duodenal ulcer, but vary in certain respects. *Perforation* of a chronic gastric ulcer along the lesser curvature is nearly always so gradual that the liver or pancreas walls off the lesion so closely that a general peritonitis does not occur. On the other hand, perforations of so-called acute gastric ulcers close to the pylorus are nearly all duodenal perforations. These free perforations into the peritoneal cavity follow the same course, whether they originate on the duodenal or gastric side of the pyloric vein. *Obstruction* may occur either at the pylorus or, rarely, at an hourglass constriction. In this series, no cases of the latter type were observed. It should also be noted that though reflex vomiting is common with gastric ulcer, pyloric obstruction significant enough to be noted by x-ray examination is much more likely to be due to duodenal ulcer or gastric cancer than it is to gastric ulcer. The demonstration of a gastric ulcer by x-ray study combined with the clinical findings of partial or total pyloric obstruction is therefore an absolute indication for operation. *Hemorrhage* is by far the most common and important complication, occurring as massive bleeding in almost exactly

the same proportion of cases as with duodenal ulcer.[10]

A history of hemorrhage of varying degrees of severity was encountered in approximately 30 per cent of this series. On the other hand, evidence of recent bleeding was found in only 16 per cent of the cases. The majority of patients entering with hemorrhage demonstrated by a hemoglobin of less than 10 gm. per 100 cc. or a red-cell count below 3,000,000 that they had bled severely. The history and further laboratory studies indicated that the anemia was the result of a slow, persistent blood loss in many cases. In the remainder, a total of 46 cases, the hemorrhage had been sudden and massive.

It is extremely important, from a surgical point of view, to segregate these patients with massive hemorrhage. For it is in this group that emergency surgical procedures must often be undertaken as life-saving measures. Although a complete discussion of the management of upper gastrointestinal hemorrhage is impossible in this short survey, the salient features of bleeding gastric ulcers may be noted.

During this period, the attitude toward these cases in the Massachusetts General Hospital has been essentially conservative. Quite in contrast to Stewart's[11] aggressive attack, these patients on the wards usually have been admitted to the Medical Service. If bleeding did not stop, or if it recurred, surgical consultation was requested. This simple plan has, in practice, been subject to so many delays that occasionally lives have been lost before operative measures have been instituted. The liaison has been much closer in the private sections so that operative delay has been less. This diversity of opinion has, perhaps fortunately, provided two distinct categories of treatment: one in which operation is reserved for patients whose hospital course demonstrates that they will die otherwise, and the other (described previously by Allen[10]), which nearly always demands early operation in the patients over forty-five years of age.

Several facts that have emerged may be stated. The history of a previous hemorrhage does not aid in the determination of the severity of the present episode. Likewise, bleeding that is apparently trivial on entry may develop into massive hemorrhage under observation. Sex does not appear to alter these factors.

The age of the patient is generally believed to be of great importance in prognosis. In this particular group, the number of patients who died from hemorrhage was so small that this factor cannot be assessed significantly. The age of the patients who recovered spontaneously without operation was fifty-seven years; that of those who required surgery to stop the bleeding was also fifty-seven years, and that of the few who died from hemorrhage was sixty-eight years. This may mean either that hemorrhage is more fatal in old age or that surgery is not requested or advised as frequently in the aged. Furthermore, the age factor is much less important with gastric ulcer, since the incidence of bleeding gastric ulcer below the age of forty-five is very low. Thus, 90 per cent of the massive hemorrhages occurred in patients over forty-five years of age. Of the patients below forty-five, one required an emergency resection, one had an interval resection, and the other recovered spontaneously; there were no deaths in this younger group.

The preoperative diagnosis of gastric ulcer in the presence of massive hemorrhage is often very difficult. Early x-ray studies will show the ulcer in about half the cases, and are of additional value in the elimination of esophageal varices, hiatus hernia or duodenal ulcer as the source of bleeding. The accuracy of x-ray study is increased by later interval examinations, but in 4 cases (9 per cent of those with massive hemorrhage), the ulcer was never demonstrated. Hence, the surgeon, at the time of laparotomy, is often confronted with a stomach that appears entirely normal. He must realize that superficial erosions, especially in the prepyloric area, may bleed massively, and that cirsoid aneurysms of the left gastric artery may rupture through microscopic ulcers in the mucosa. Obviously, in these cases, a careful pathological examination will be necessary to establish the diagnosis, and the surgeon is required to explore by a gastrotomy incision or to resect a stomach that appears grossly normal.

Fortunately, gastric resection for actively bleeding gastric ulcer is much less hazardous than that for bleeding duodenal ulcer. This is due to the lack of technical difficulty about the duodenal stump and to the fact that hemorrhage can be controlled in an absolute fashion. Despite the fact that only one of the operations in this group was carried out within forty-eight hours of onset of the hemorrhage, postoperative complications have been rare.

The results in this series may be summarized as follows: 58 patients entered the hospital with gastric ulcer and severe anemia. Four patients died of massive hemorrhage from a gastric ulcer, proved by autopsy, without operation; in retrospect it appears that early surgery might have saved 2 of them. Twenty-eight patients survived without operation, and 26 were operated on during the initial hospital admission. The condition of the majority of the patients had been improved considerably before operation, but in 9 cases operation was carried out as an emergency measure in the presence of active bleeding. There was only one postoperative death, and that followed a late attack on an ulcer that had bled repeatedly on the medical wards.

The over-all death rate from hemorrhage was therefore approximately 9 per cent. In patients

treated surgically it was 4 per cent, whereas in those treated conservatively, it was 12.5 per cent. Consequently, it appears that surgery can be carried out in this group of patients with relatively little hazard and with better results.

It is our belief that there are three groups of patients with gastric ulcer who require emergency operation. A patient admitted with massive upper gastrointestinal bleeding should be given a careful x-ray examination, palpation being avoided, as soon as stabilization has occurred. If a positive diagnosis of gastric ulcer is obtained, and the patient has been bleeding less than forty-eight hours, immediate operation is indicated. If he has been bleeding for a longer time but the hemorrhage stops soon after hospital admission, a period of observation and medical treatment is advised in the expectation that normal blood and nutritional levels may be reached and gastric resection carried out at a time of election. Immediate operation is indicated in this group if a recurrent hemorrhage occurs at any time. In a third, small group, the gastric hemorrhage fails to stop after the patient arrives in the hospital, and operation is indicated soon after his arrival. The same operative indications hold true in the absence of a positive x-ray diagnosis of ulcer provided pathologic lesions of the esophagus, especially varices, and blood dyscrasias can be excluded.

Operations for Gastric Ulcer

Indications

If it is conceded that any gastric ulcers are to be treated medically, it would be well to define as accurately as possible the groups of patients that are likely to do well and those that will do poorly on conservative therapy. Unfortunately, this is impossible, except in very general terms. An analysis of all the features of the two groups shows that they are nearly exactly similar, and that it cannot be foretold in the great majority of cases what the response to therapy will be. Thus, the sex and age distributions, the location of the ulcer, the incidence of achlorhydria and the presence of occult blood in the stools are strikingly similar. It does appear that the particular ulcers that do poorly on medical treatment are the larger ones, particularly those that are over 2.5 cm. in diameter, those that are associated with obstruction, and those that are recurrent with a long history of gastric symptoms.

It is suggested, therefore, that a trial of medical therapy be reserved for patients in whom an excellent radiologist and gastroscopist indicate that the ulcer is grossly benign and who have a duration of symptoms of less than one year, an ulcer that is 1 cm. or less in diameter, located on the lesser curvature, and a negative cytologic smear. If the x-ray diagnosis is equivocal or not of the highest quality, ulcerative lesions in a stomach with histamine achlorhydria or those that are found elsewhere than on the lesser curvature or high in the cardia should also be singled out for immediate surgery. It will be observed that patients with ulcers in the cardia are permitted a period of medical therapy despite the fact that the incidence of cancer is high; this is done because the operative mortality for lesions in this particular location is still great enough to counterbalance the error in diagnosis of cancer. The failure of any of these ulcers to heal, as stressed above, is an absolute indication for surgery.

Types

Any operative procedure for gastric ulcer must satisfy two criteria. It must change the gastric physiology in such a fashion that recurrent ulceration cannot follow, and it must be extensive enough that an adequate operation will have been done if cancer is found on microscopical examination of the specimen. It follows that such operations as gastroenterostomy and vagotomy have no place in the treatment of gastric ulcer, and that some type of gastric resection is indicated when surgery is undertaken.

A satisfactory resection consists of the excision of an adequate section of stomach on either side of the ulcer together with the regional lymph nodes along both curvatures. We believe this is accomplished most satisfactorily by the removal of both the greater and lesser omenta together with at least 50 per cent of the stomach. Furthermore, it has been found that sleeve resections are not satisfactory because the gastric physiology is not altered sufficiently and a recurrent ulcer may occur. Clinical experience has shown that the antral mucosa exerts a great influence on gastric secretion. Thus, if a Finsterer exclusion procedure is carried out for duodenal ulcer, with the line of distal section through the antrum, and with retention of the antral mucosa, a postoperative jejunal ulcer can be expected in nearly every case. It is obvious that this operation is used very rarely for gastric ulcer, since it is usually easier to divide the duodenum. However, it was employed in one case in this series, and the patient thereafter developed a recurrent gastric ulcer near the anastomosis. Relief followed resection of the retained antrum. The importance of the antrum has been confirmed by Ransom,[12] who reported 4 anastomotic ulcers following gastric resection for gastric ulcer, and in 3 of them the resections were incomplete since the antral mucosa was retained.

Resection of the distal portion of the stomach, including the ulcer and at least 2 cm. of normal mucosa proximal to it, is possible in most cases. If a narrower margin is necessary because of the proximity of the esophagus, immediate pathological examination with a frozen section is advisable. We

agree with Marshall and Welch[13] that mobilization of the left gastric artery often makes an apparently high ulcer relatively easy to resect. However, there remains a group of ulcers near the cardia and in the fundus that cannot be excised by this method, and it is this group that now can be treated adequately by resection of the proximal portion of the stomach.

The high ulcers include about 10 per cent of all gastric ulcers. As noted above, increasing experience with this group has shown that the differential diagnosis of cancer over the ulcer is especially difficult in this section of the stomach. Heretofore, only two solutions have been available — total gastric resection and distal partial gastric resection with retention of the high ulcer.

Total gastric resection has been employed, and will continue to be used for certain gastric ulcers that are believed to be extensive carcinoma. The end-results prove, however, that this operation is to be avoided, when possible, for benign lesions.

TABLE 3. *Operative Mortality.*

OPERATION	NO. OF CASES	NO. OF DEATHS	MORTALITY
			%
Partial distal gastrectomy	269	6	2.2
Partial proximal gastrectomy	14	3	21.0
Total gastrectomy	4	0	0
Miscellaneous	8	0	0
Totals	295	9	
Average			3.0

Varying degrees of malnutrition and anemia, as pointed out by MacDonald, Ingelfinger and Belding,[14] occur postoperatively and have, in certain cases, proved troublesome.

Since the antral mucosa is so important in the formation of ulcers, Madlener[15] suggested that a resection of the distal stomach could be done for a high ulcer with the expectation that it would heal spontaneously thereafter. The operation was revived by Colp,[16] who reported favorable results in 8 cases. This procedure has not found favor elsewhere since it not only fails to eliminate the possibility of cancer but also has not affected healing in certain cicatrized ulcers.

More recently two other methods of attack have been developed. Vagotomy has been suggested as of particular value in the inaccessible group of ulcers. This procedure may give a false sense of security that is quite unjustifiable. We cannot agree that it has any place in the treatment of the lesions that frequently turn out to be cancer.

The final method appears the most logical in this group. It involves a proximal partial gastric resection, including the ulcer, with an esophagogastric anastomosis. Developed concomitantly with the operative attack on carcinoma of the cardia and lower esophagus, Churchill and Sweet[17] have described the technic that is followed for all lesions in this location. In this series, 14 cases of high gastric ulcer have been treated by this method, chiefly by Dr. Richard H. Sweet.

Theoretically, this operation has several features that will make the late follow-up results of great interest. Thus, the antral mucosa is retained—definitely a hazard in any other type of ulcer operation. Since a vagotomy is automatically done by the nature of the operation, as well as a removal of a large portion of the acid-bearing fundus, it is probable that the ultimate results will prove satisfactory. Studies of gastric secretion of several of these patients are now under investigation by Jones and Culver[18] and will be reported later by them.

Removal of these high ulcers by proximal resection is accompanied by a greater risk than that of partial distal resection and is followed by more postoperative symptoms. Follow-up results have been obtained in 10 of the 11 patients who survived operation. There are no recurrent ulcers in the group. Four are entirely asymptomatic. The others complain of various symptoms that are trivial in 4 and severe in 2. They consist of fullness on the ingestion of small amounts of food, and regurgitation of small amounts of mucus and bile early in the morning.

Complications and Mortality

With the exception of the fatal cases, the postoperative complications were, in general, of little importance. The mortality of partial distal gastric resection was 2.2 per cent (Table 3). The 6 deaths were due to local sepsis (2 cases), pneumonia (2 cases), acute pancreatitis (1 case) and appendicitis with perforation (1 case). After transthoracic partial proximal resection the mortality was 21 per cent. There were 3 deaths: 1 patient succumbed of postoperative shock, 1 of coronary thrombosis, and 1 (who also had a resection for carcinoma of the esophagus) of massive pulmonary embolism.

RESULTS

With the exception of the proximal partial gastric resections, no elaborate attempt has been made to carry out complete follow-up studies in this group of patients, since this work is in progress and will be reported elsewhere.[19] The general trends of conservative therapy, however, are indicated in the following figures, comprising the years 1940–1946. Eleven per cent of the entire group of patients did well on medical therapy. In 14 per cent the results were probably good, but were indeterminate since the patients did not return long enough to the outpatient department for us to be sure that the ulcer remained healed. Twenty per cent did poorly and refused further treatment or required surgery.

Surgical therapy was carried out at some time in 58 per cent of the entire series. A small group of 8 patients had miscellaneous operations. Two

had a vagotomy; 1 is apparently cured, whereas the other has a recurrent ulcer. Gastrotomies were carried out in 2 patients, no ulcer being demonstrated; one of them did well, and the other has radiologic and clinical evidence of recurrent ulcer. Three patients had a gastroenterostomy; one of them died later, probably of cancer, another had a massive hemorrhage two years later, and the third has been lost. One patient who had a local excision of an ulcer for massive hemorrhage did well.

Gastric resections were carried out in 295 cases. Four of the patients had a total gastrectomy — loss of weight and inability to maintain nutrition are common in this group. The remainder had partial gastrectomies. After recovery from resection, only 1 patient has required reoperation. That patient, mentioned above, developed a recurrent gastric ulcer following a Finsterer exclusion procedure for massive hemorrhage. One patient developed an anastomotic ulcer two years after an adequate subtotal gastrectomy. This jejunal ulcer responded rapidly to medical therapy. The possibility of an anastomotic ulcer was raised in 3 other cases, but in none could a crater be discovered on x-ray examination and all patients recovered promptly on conservative therapy.

Follow-up studies, still incomplete, indicate that approximately 75 per cent of the patients will be asymptomatic after partial gastric resection. Fifteen per cent will have trivial gastric symptoms, easily controlled by diet. Ten per cent will have symptoms of a small stomach, lack of appetite or gastric distress and loss of strength, endurance or weight that will require medical care. These conclusions agree with those of Ransom,[12] but are slightly less favorable than those of Walters and Clagett,[20] who report uniformly excellent results after subtotal resection for gastric ulcer.

Summary and Conclusions

Several trends in the management of gastric ulcer have become apparent in the past few years. It has been shown that the term "peptic ulcer" should be eliminated, and that gastric ulcer is a distinct entity not to be confused with duodenal ulcer. It has also been demonstrated that gastric ulcer still cannot be differentiated from cancer in nearly 10 per cent of the cases. Although improved diagnostic methods have tended to reduce this error, the mortality of operation has simultaneously declined to minimum levels.

To the surgeon interested in cancer control, these tendencies make gastric resection advisable for all gastric ulceration. The physician, on the other hand, is tempted to treat these ulcers medically, stressing the operative mortality, low though it may be, the discomforts of operation and the post-gastrectomy symptoms that may appear.

If medical therapy is elected, such cases must be carefully selected, studied by the best radiologist and gastroscopist available, and followed vigilantly, with early recourse to surgery if healing is not prompt. The physician must realize that new operative technics provide satisfactory excisional surgery for ulcers of the cardia and that radical surgery for the most common complication of gastric ulcer — hemorrhage — is both safe and desirable.

From the principles outlined above, it appears that surgical therapy is indicated in approximately 75 per cent of the patients with gastric ulcers and that excellent results are to be expected after gastric resections.

References

1. Holmes, G. W., and Hampton, A. O. Incidence of carcinoma in certain ulcerating lesions of stomach. *J. A. M. A.* **99**:905-907, 1932.
2. Sproull, J. Discussion of occurrence of benign ulcer on greater curvature. *Am. J. Roentgenol.* **25**:464-473, 1931.
3. Allen, A. W., and Welch, C. E. Gastric ulcer: significance of this diagnosis and its relationship to cancer. *Ann. Surg.* **114**:498-509, 1941.
4. Schatzki, R., and Eyler, W. R. Personal communication.
5. Papanicolaou, G. N. Diagnostic value of exfoliated cells from cancerous tissues. *J. A. M. A.* **131**:372-378, 1946.
6. Graham, R. M., Ulfelder, H., and Green, T. R. Cytologic method as aid in diagnosis of gastric carcinoma. *Surg., Gynec. & Obst.* **86**:257-259, 1948.
7. Fisher, A., Clagett, O. T., and McDonald, J. R. Coexistent duodenal ulcer and gastric malignancy. *Surgery* **21**:168-174, 1947.
8. Eusterman, G. B., and Balfour, D. C. *The Stomach and Duodenum.* 958 pp. Philadelphia: W. B. Saunders Co., 1935.
9. Lahey, F. H. Discussion of Ransom.[12]
10. Allen, A. W. Acute massive hemorrhage from upper gastrointestinal tract: with special reference to peptic ulcer. *Surgery* **2**:713-731, 1937.
11. Stewart, J., Massover, A. J., Potter, W. H., and Schaer, S. M. Massive hemorrhage from gastroduodenal ulcer. *Surgery* **24**:239-245, 1948.
12. Ransom, H. K. Subtotal gastrectomy for gastric ulcer: study of end results. *Ann. Surg.* **126**:633-654, 1947.
3. Marshall, S. F., and Welch, M. L. Results of surgical treatment for gastric ulcer. *J. A. M. A.* **136**:748-752, 1948.
14. MacDonald, R. M., Ingelfinger, F. J., and Belding, H. W. Late effects of total gastrectomy in man. *New Eng. J. Med.* **237**:887-896, 1947.
15. Madlener, M. Über Pylorektomie bei pylorusfernem Magengeschwür. *Zentralbl. f. Chir.* **50**:1313-1317, 1923.
16. Colp, R., and Druckermann, L. J. Palliative gastrectomy in selected cases of gastric ulcer. *Ann. Surg.* **124**:675-687, 1946.
17. Churchill, E. D., and Sweet, R. H. Transthoracic resection of tumors of stomach and esophagus. *Ann. Surg.* **115**:897-920, 1942.
18. Jones, C. M., and Culver, P. Unpublished data.
19. Moore, F. D., et al. Unpublished data.
20. Walters, W., and Clagett, O. T. Surgical treatment of chronic gastric ulcer: review of two hundred and seventy-two cases. *Surg., Gynec. & Obst.* **71**:75-79, 1940.

PULMONARY HAZARD OF THE INGESTION OF MINERAL OIL IN THE APPARENTLY HEALTHY ADULT

A Clinicoroentgenologic Study, with a Report of Five Cases

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PERIODIC reports of harm resulting from the ingestion or aspiration of mineral oil have appeared in the medical literature and even in the lay press. Recently, it has been shown that the taking of liquid petrolatum with food prevents substantial amounts of food carotene, a precursor of vitamin A, from entering the body.[1] This fact and some corollaries thereto have been established to the satisfaction of authors of the latest books on nutrition and vitamin therapy and have provoked editorial comment.[2]

More than two decades have elapsed since it was demonstrated that serious harm can be done to the lungs by the introduction of mineral oil into the nose or throat in pure form or as a vehicle for other medicaments.[3] This source of chronic aspiration pneumonitis, or so-called lipid pneumonia, was described as occurring especially in infants and young marantic children.[4] The use of this hydrocarbon in nose and throat medication was thereupon officially condemned by the New York City Health Department. Soon, intranasal instillation of liquid petrolatum was shown to be equally harmful to adults and children,[5] and the reversibility of the pulmonary process following the withdrawal of this treatment was demonstrated.

Then it was found that a chronic pneumonitis can be induced by ingestion of mineral oil as a laxative over a long period. Characteristic pulmonary lesions were encountered in debilitated, recumbent and aged persons, in persons suffering from dysphagia of nervous origin and in patients in whom neoplastic or other destructive processes involved the mouth or throat. This accounts for the large series of cases of lipid pneumonia reported from hospitals for the chronically sick[6] and the aged and infirm,[7] and wisely led to the abandonment of the use of mineral oil as a habitual laxative for these patients. It is interesting to note in this connection that liquid petrolatum as a laxative has accounted for nearly half the adult cases of oil-aspiration pneumonia reported thus far and that half the series of 264 cases of this pulmonary disease compiled by Sweeney[8] in 1942 were found in adults.

It is the purpose of this paper to emphasize the pulmonary hazard to apparently healthy and ambulatory adults inherent in the habitual use of mineral oil by ingestion. Indeed, the bronchopulmonary process in these persons comes on so insidiously that it may be uncovered only on a tuberculosis case-finding x-ray survey. It is not a new clinicoroentgenologic phenomenon that prolonged ingestion of this hydrocarbon for laxative or other purposes (one patient said he took mineral oil for the tonic effect it had on him — he called it "poor man's olive oil") can cause chronic pneumonitis in the apparently healthy adult. Individual cases in which the diagnosis has not been made ante mortem or preoperatively have been reported even till recently. Commonly if the pneumonitis is one sided in these older adults, the examining physician often makes a diagnosis of bronchogenic carcinoma,[9,10] only to find evidence of oil-aspiration pneumonia in the removed lung specimen. It is to be hoped that the index of suspicion of this insidious man-made disease will increase. It is reasonable to conclude that many cases of benign pneumonitis in the apparently healthy are going undetected if 5 such patients have been seen by one observer in a two-year period.

Recently, 2 cases of oil pneumonitis in healthy adults who were normal neurologically except for the finding of an absent gag reflex were reported.[11] In 2 other cases, cited below, the gag reflex was markedly diminished, and in still another some dysphagia was associated with the presence of a Zenker diverticulum. Although careful examination of the throat in apparently well older persons might show some abnormality causing the spilling over into the larynx of ingested liquid petrolatum, it has been demonstrated that this substance is so bland that, introduced into the nasopharynx, it can find its way into the lungs without causing symptoms of irritation, such as cough.[12] Serial x-ray films in these cases indicate that it probably takes a long time for a radiologically visible reaction to occur in the lung into which oil aspiration has taken place. Once developed, however, the pneumonitis slowly increases as long as the patient continues on the oil laxative regime. In these apparently healthy persons, only a minute quantity of the oil gets down into the lower order of bronchi at one time, and as time goes on some of it is fortunately removed by expectoration and to a lesser degree by phagocytosis. One patient with lipid pneumonia exhibited no roentgenologically detectable trace of this product in his bronchi shortly after ingestion of 20 cc. of iodized oil.

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Pathology and Pathogenesis

A brief description of the pathology of chronic pneumonitis due to mineral oil follows, to call attention to the factors that will enable one to make a clinical diagnosis in the ambulatory adult. It has been shown that the severity of the reaction in the lung to aspirated oil depends upon the character of the oil.[13, 14] When saponifiable oils enter the lower respiratory tract, the type of immediate reaction is due to the amount of fatty acid present or produced from the aspirated oil by tissue enzymes. Mild vegetable oils, like poppy-seed oil, olive and sesame oils cause the least reaction. On the other hand, cod-liver oil, lard and animal fats are capable of producing sudden and violent reactions, with hemorrhage and necrosis. The response of the lung to liquid petrolatum, a nonsaponifiable oil, is extremely mild, amounting to a foreign-body reaction to an inert substance within and around the alveoli in which the oil settles. The final stage in this pathologic process is fibrosis of the lung occurring first as a mere thickening and infiltration of the alveolar septum and later going on to form fibrous nodules, some tubercle-like, around large collections of lipoid material. A proliferative rather than a necrotizing pneumonia is the rule after repeated aspiration of liquid petrolatum. Occasionally, the proliferative pneumonitis takes on the pathological and x-ray appearance of a circumscribed, uniformly dense tumor mass surrounded by a concentric fibrotic ring to which Ikeda[15] has given the name "paraffinoma."

The presence of free oil in the alveoli in pneumonitis due to mineral oil is so striking that oil may be found at the surface of the preserving fluid shortly after a cut section of the involved lung is placed in a laboratory jar containing the fluid. This phenomenon helped to focus the attention of pathologists on the existence of this uncommon disease.

Microscopically, macrophages filled with oil may be found in the alveolar spaces, in the lymphatics and in the hilar lymph nodes. The last, however, are rarely appreciably enlarged even in the later stages of oil-aspiration pneumonia. Pleural reactions, too, are extremely uncommon, and if they occur are usually secondary to superimposed infection.

It is not difficult to see that the disposition of the aspirated oil is dependent largely upon gravity and inspiration suction. Accordingly, the mineral-oil pneumonitis in the ambulatory adult will be found as a rule at the lung bases, more on the right than the left, and ultimately in both lower-lung fields.

Symptoms, Signs and Course

A remarkable paucity of symptoms referable to the respiratory tract is elicited on close questioning, even when the pulmonary involvement is far advanced. Certainly the patient is asymptomatic when the process in the lungs is in its incipiency. It is uncommon for this low-grade pneumonitis to be complicated by symptoms of suppuration of the lungs or bronchiectasis. As might be expected, some of the patients may be subjected to recurrent acute pneumonias superimposed upon the oil pneumonitis. As the pulmonary reaction to the liquid petrolatum piles up to an imposing radiographic appearance, the patient becomes noticeably dyspneic on exertion and may develop a hacking cough. However, because of age, the dyspnea and cough may be attributed to arteriosclerotic heart disease. Or, if the pulmonary disease is discovered for the first time on x-ray study and found to be one sided, a diagnosis of carcinoma of the bronchus may be made.

The striking thing about this benign disease in most ambulatory adults is the good nutrition, comfort and general well-being of the patient in the presence of even extensive pulmonary involvement. Likewise, it is also remarkable that, given the x-ray findings in a proved case of mineral-oil pneumonitis, re-examination of the involved lungs will disclose only scant and unrevealing signs on inspection, percussion and auscultation.

Fluoroscopy and Chest X-Ray Study

The earliest involvement of the lungs by the chronic aspiration of liquid petrolatum causes no localized findings on the chest film or only increased markings. As the oil continues to spill over into the lungs, a small, basal, infiltrative process, looking not unlike a bronchopneumonic lesion, soon appears. At times, the early process seen on the x-ray film has a hard appearance, owing to the intense proliferative reaction around the oil-containing alveoli. The picture, as in one of the cases reported below, may resemble that seen long after bronchography has been done with a radio-opaque oil in the pulmonary area, and a fine residuum of that substance has been left.

As the pneumonitis progresses, the infiltrations fuse into an ill defined area of ground-glass density, or the density may become circumscribed (paraffinoma formation). As a rule, no associated indirect evidence of atelectasis is apparent, nor is hilar adenopathy noted. The latter features are worth bearing in mind in the differentiation of this benign disease from a neoplastic process.

On fluoroscopy, both leaves of the diaphragm move freely, their contour is not appreciably altered, and the heart and the mediastinum are situated in the normal position. Diaphragmatic changes will occur, however, in late oil pneumonitis as a result of secondary infection and compensatory emphysema.

In these ambulatory patients, radiographic extension of the lesion is to be expected as is ultimate involvement of both lung fields while the patient continues on the oil regimen. A sudden regression

in the extent of the lesion under these circumstances is usually due to a subsiding acute pneumonitis superimposed upon the chronic process. Once the acute infection is over, the proliferative lung disease will continue its very slow progress. With the discontinuance of this type of laxative habit, early infiltrations have been seen to clear up. However, the large lesions change little radiographically for years after oil aspiration has ceased.

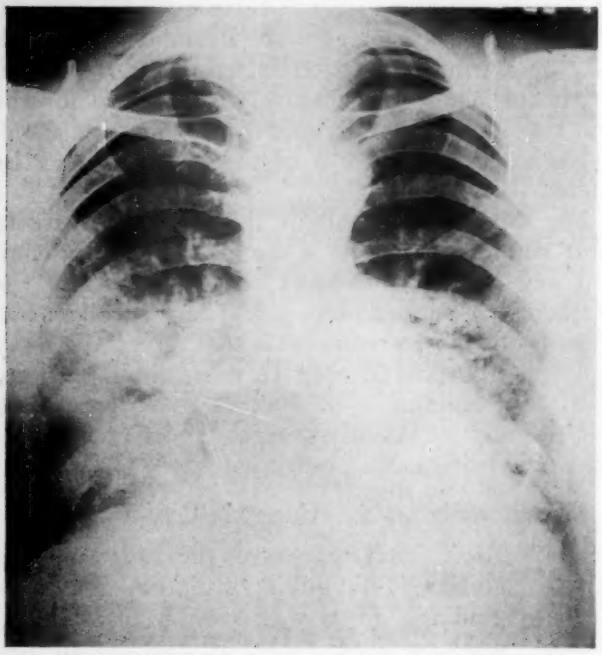

FIGURE 1. *Roentgenogram in Case 1.*

DIAGNOSIS

Until now the diagnosis of lipid pneumonia has been too frequently a pathological one. In view of the experience presented below, more of these cases will undoubtedly be uncovered by case-finding surveys. With the extension of chest screening to general-hospital admissions, still more cases of oil-aspiration pneumonitis with few symptoms should be uncovered if the index of suspicion of this phenomenon runs high. The importance of making the diagnosis cannot be too strongly stressed, among other reasons, lest a case of this sort be sent to the surgeon for needless lobectomy or pneumonectomy.

A history of regular ingestion of mineral oil should be inquired into when one is dealing with a basal process of undetermined etiology in an otherwise well adult. Certainly, the suspicion of chronic benign pneumonitis due to liquid petrolatum must be seriously considered in the presence of a bilateral lower-lobe process found on a routine chest film of an adult who has few respiratory complaints and who exhibits few physical signs on examination of the thorax.

The chief difficulty in differential diagnosis occurs when the lesion is unilateral. Then the possibility of neoplasm is uppermost in the mind of the present-day clinician. Contrary to bronchogenic carcinoma, however, in this chronic benign process the x-ray film reveals the lesion to extend peripherally; atelectatic phenomena are absent, and hilar adenopathy is not usually seen. Although carcinoma of the lower respiratory tract can exist with relatively few symptoms referable to the lungs, the cause of the process is less likely to be neoplasm than oil-aspiration pneumonitis, in which negative bronchoscopy is the rule unless there has been supervening infection.

The differentiation of lipid pneumonia in the adult from basal tuberculosis, primary bronchiectasis or mycotic bronchopulmonary infection is a less difficult task. In these ailments, the symptoms, signs and difference in x-ray shadows are usually in sharp contrast to those of oil-aspiration pneumonitis. In addition, the examination of the sputum for specific organisms and the character and quantity of the expectoration will clinch the diagnosis of these chronic infections.

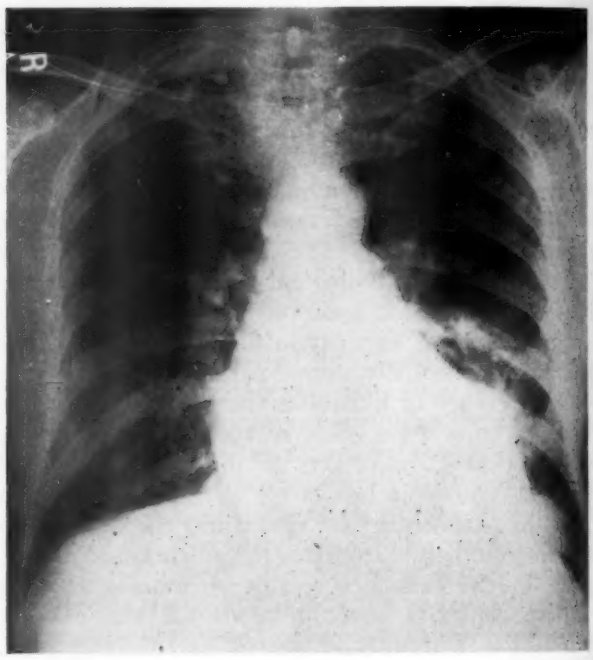

FIGURE 2. *Routine Film of the Chest Taken on June 10, 1944, in Case 2, Showing an Ill-Defined Infiltration Under and Adjacent to the Left Heart Border and Also an Old, Minimal Lesion at the Right Apex.*

Two certain confirmatory tests have been used in the diagnosis. Both are based on the pathological finding that mineral oil remains in the alveoli long after aspiration into the affected lung has ceased.

The first test is an examination of the sputum for oil droplets. This procedure should be carried out some days after the patient has ceased taking mineral oil. Into a clean, wide-mouthed jar, the patient expectorates before breakfast for three successive days after thoroughly washing his mouth and throat with physiologic saline solution. He keeps this jar in the refrigerator concealed in a paper bag so that the contents do not offend the ice-box raider. Two analyses may then be done with this accumulated sputum. If oil droplets are present, placing cigarette paper or a piece of lens paper on the surface of the expectorated material will bring out the tell-tale grease spots on the paper. Now, if a sample of the sputum is examined under the microscope, the contained mineral oil droplets will take the characteristic stain with scarlet red. Saponifiable fats and oils, on the other hand, take the osmic acid stain.

The second confirmatory test is an aspiration biopsy of the affected lung. This procedure when wisely employed is comparatively safe,[7, 16] the chief danger and discomfort being the induction of a pneumothorax. The region to be punctured is carefully mapped out under fluoroscopic control. Procaine is injected into the skin, and a needle of 16 or 17 bore is plunged quickly into the involved lung parenchyma. Suction should then be applied until a little bloody material is drawn into and mixed with the procaine in the barrel of the syringe. The needle is then just as quickly withdrawn. Holding the syringe vertical for a while against a bright light with the needle upward, one can see oil droplets on the surface of the bloody fluid if the biopsy has been properly performed in a case of lipid pneumonia. To determine if the oil seen is liquid petrolatum, microscopical examination may then be performed with the use of scarlet-red stain.

Treatment

It is clear that the ambulatory adult found to have oil-aspiration pneumonitis is promptly told to discontinue taking mineral oil. As indicated above, early lipid pneumonia changes will ultimately resolve if this source of lung irritation is stopped in time and if there is no neurologic or anatomic defect in the nasopharnyx, promoting additional insults to the already damaged pulmonary tissue. Occasionally, a Zenker diverticulum will be found acting as a reservoir for the spilling over of oil into the lower respiratory tract.[17] This should be appropriately treated.

If there is superimposed pulmonary suppuration or bronchiectasis, the treatment may well be the surgical extirpation of the involved lobe or lobes in patients who are good surgical risks. Lobectomy may also be a wise procedure when a patient with proved oil pneumonitis suffers recurrent attacks of acute bronchopneumonia on top of a one-sided lesion whose likelihood of clearing up after the discontinuance of the oil habit is remote. A less common indication for radical treatment is the concurrent or possibly subsequent development of alveolar cell carcinoma.[18]

Case Reports

The following is a brief presentation of 5 cases of oil-aspiration pneumonitis with the pertinent clinicoroentgenologic data. Curiously enough, all patients were men in their sixties; 4 cases may be said to have been picked up on survey chest films, and the benign course of 3 cases has been followed for some time.

Case 1. H. K., a 67-year-old retired laundry-truck driver, had never had a chest x-ray examination until visited by a mobile survey unit in May, 1948. He had had a slight cough, which was often spasmodic, for about 20 years. He expectorated a small amount of greenish, nonodorous sputum daily. There was no appreciable dyspnea on exertion or orthopnea. He was subject to infrequent colds associated with a slight fever lasting a few days once or twice a year. No weight change had been noted over the course of years. On the basis of fluoroscopic examinations recently performed, he was told by his physician that the lung changes noted were due to a failing heart.

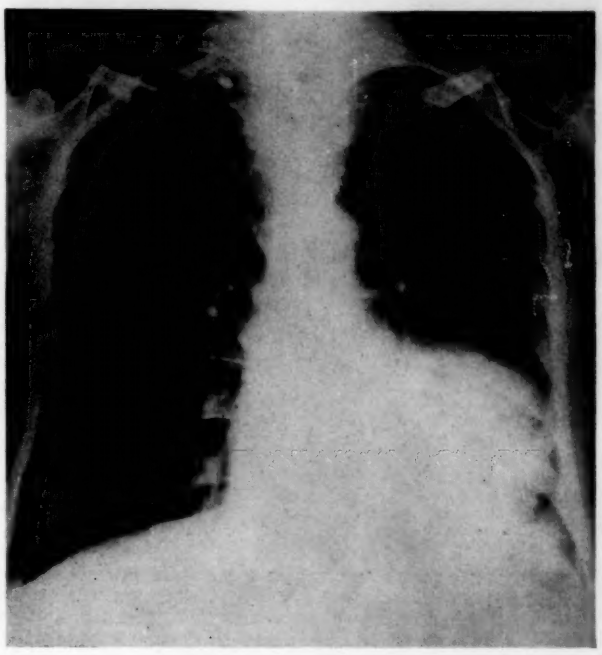

Figure 3. *Film Taken in Later Examination in Case 2.*

He had been taking 2 or 3 tablespoonfuls of mineral oil almost daily for the relief of constipation for the past 25 years. He was in the habit of drinking the oil directly from the bottle, and took this medication during the day as well as before retiring. He did not use nose drops. He did not gag or choke when taking anything by mouth.

Physical examination on June 29 disclosed a patient who did not appear acutely or chronically ill. There was moderate clubbing of the fingers and some cyanosis. No cardiac abnormalities were found. Examination of the chest revealed diminished breathing at the right base; no rales were heard. The gag reflex could hardly be elicited.

X-ray study of the chest showed a diffuse conglomerate infiltration in the lower half of both lungs, denser and more marked on the right side (Fig. 1). There was a suspicious area of central necrosis within the right basal lesion. On fluoroscopy both leaves of the diaphragm appeared smooth and moved freely. The right costophrenic sinus was obliterated.

Examination of the blood revealed a slight secondary polycythemia. The sputum was negative for tubercle bacilli.

Some days after the ingestion of oil had been discontinued,

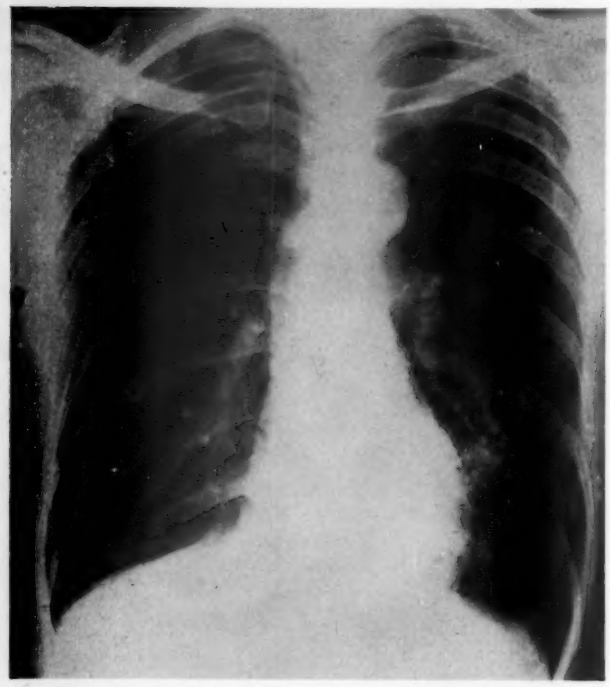

FIGURE 4. *Roentgenogram in Case 3.*

the patient was asked to bring in some sputum for examination for liquid petrolatum, in accordance with the procedure outlined. The sputum was thick and greenish and had no odor. The presence of mineral-oil droplets was readily demonstrated microscopically.

This was probably a long-standing case of lipid pneumonia. Secondary suppuration was undoubtedly present, characterized by the expectoration of purulent sputum, the x-ray picture of the right base and the clubbing of the fingers. The typical distribution of the process in this ambulatory patient and the paucity of physical signs are worth noting, as is the ease with which mineral oil was found in the sputum.

CASE 2. E. Y., a 64-year-old unemployed laborer, had had numerous hospital admissions for nondisabling rheumatoid arthritis and had recently developed arteriosclerotic heart disease with congestive failure. At present he was an ambulatory patient receiving weekly injections of mercurial diuretics and complained of nothing more than some dyspnea on exertion.

During one of his sojourns in the hospital a routine chest film done on June 10, 1944, revealed, in addition to the presence of a slightly enlarged heart, a scattered infiltrative process adjacent to the left cardiac border that appeared to be emerging from underneath the left side of the heart (Fig. 2). There was also an old, minimal, fibrocalcific tuberculous lesion at the right apex. No respiratory symptoms or lung signs were noted at that time. At a later admission during the summer of 1947 the patient complained of a slight cough, and a chest film showed a very large, uniformly dense and sharply circumscribed lesion (Fig. 3) in the left-lower-lobe area, the infiltration in the lobe having coalesced and giving the appearance of a uniformly dense, discrete mass (paraffinoma). A provisional diagnosis of bronchial neoplasm was made. Bronchoscopy showed only a thickened, congested and narrowed left bronchus, and a Papanicolaou smear of the sputum was negative.

When this patient was seen on a routine visit in April, 1948, the examiner was impressed with the fact that the left basal lesion had progressed only slightly on serial x-ray study since the preceding July. Furthermore, the patient looked too well and comfortable for a person ill with a bronchial carcinoma of that size of at least 1 year's duration. Close questioning disclosed that he had been taking 2 tablespoonfuls of mineral oil regularly at night for the previous 10 years. He was thereupon readmitted to the hospital for aspiration biopsy of the left lower lobe under fluoroscopic control, according to the method outlined above. He stood the procedure well, and there were no ill aftereffects. Free oil droplets were easily found in the fluid withdrawn from the lung on both gross and microscopical examination.

In this case the growth of the lipid-pneumonia lesion could be traced on the x-ray film from its

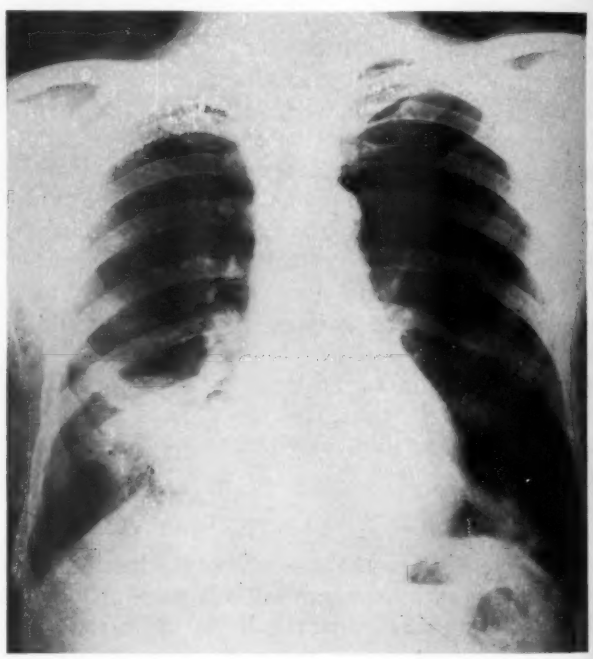

FIGURE 5. *Roentgenogram in Case 4.*
The mesh-like fibrosis in the right middle lobe, as well as above the left leaf of the diaphragm, presents a different appearance from that in the previous cases.

early beginnings as a nondescript basal infiltration to subsequent discrete tumor formation. The ease with which free oil was found on needle biopsy that helped clinch the diagnosis is also worth noting. If the disposition of the aspirated oil depends on gravity one expects the basal pneumonitis to be more likely on the right than the left side. A possible explanation for the fact that the pulmonary involvement was located exclusively on the left

may be that he invariably went to sleep on his left side shortly after taking his usual nightcap of mineral oil.

CASE 3. S. D., a 60-year-old Negro porter, first came under observation when given a routine x-ray examination in an effort to trace the possible source case to his son, who had died of pulmonary tuberculosis in January, 1948.

The patient had no cough or other respiratory symptoms. His appetite had been good. His occupation had always been that of porter. There had been no exposure to noxious dusts. He had not been using nose drops. For the past three winters he had been in the habit of taking a tablespoonful of mineral oil daily after breakfast. He had also been taking this hydrocarbon at infrequent intervals in the other seasons of the year.

Physical examination disclosed no abnormal findings except for slight malnutrition and a markedly diminished gag reflex. The sputum was negative for tubercle bacilli and positive for oil droplets grossly and microscopically. X-ray study of the chest on May 17, 1948, showed a fine nodular lesion in the left-lower-lung field anteriorly between the level of the fourth and sixth ribs (Fig. 4). The appearance of the process was not unlike that seen some time after bronchoscopy when incompletely expectorated iodized oil has been left in a number of the alveoli.

The interesting feature of this case is that it probably represented an early completely asymptomatic oil-aspiration pneumonitis. Much less of the hydrocarbon had been aspirated into the lungs in this case than in the previous ones. All that is needed here is the prompt recognition of the cause of the pulmonary lesion and asking the patient to desist from taking any more mineral oil. In view of the paucity of the pulmonary reaction there is a likelihood that the left-lung lesion will become reversible to a great extent after some time once the oil ingestion habit has ceased.

Unfortunately, the recovery of oil in the sputum or by lung puncture in the following 2 cases could not be obtained, owing to nonco-operation. However, the clinicoroentgenologic course, the history and the very long follow-up study have left no doubt in my mind, or in those of many groups of radiologists and phthisiologists to whom the films have been shown, that these are also excellent examples of insidiously developing pulmonary granulomas due to chronic aspiration of mineral oil taken for laxative purposes.

CASE 4.* H. S., a 63-year-old real-estate operator, had been followed for 2 years since the discontinuance of the mineral-oil habit.

The pulmonary lesions had been discovered in a case-finding survey done on June 17, 1946. This film and an oblique view taken on the same day showed a large area of ground-glass density confined to the right middle lobe and a small, less well defined area of similar character in the left-lower-lobe region just above the diaphragm (Fig. 5). A diagnosis of carcinoma of the lung was made elsewhere, and the patient was in a greatly wrought-up condition over the concern shown him because of the accidental findings in the chest film.

It was believed that the bilateral process spoke against carcinoma, as did also the almost complete absence of symptoms and signs and the apparent excellent preservation of health. An absent gag reflex was also noted.

On careful questioning the patient gave a history of taking mineral oil for constipation for the past 20 years. Hardly a day had passed, according to this patient, without his taking about 2 ounces of liquid petrolatum, which he often drank from the bottle. This preparation was consumed both day and night. He took no nose drops and had no dysphagia.

A film taken 2 years after the discontinuance of the mineral-oil habit showed no appreciable change in the extent or character of the pulmonary lesions that had been revealed on the original x-ray survey. His general health remained excellent.

*This case has been reported elsewhere.[11]

The diffuse fibrosis characterizing this case of long-standing oil pneumonitis is obviously not reversible, as indicated by serial films taken over a two-year period. Nevertheless, since the patient discontinued taking liquid petrolatum his health has remained good, and he has had no intercurrent illnesses, respiratory or otherwise. Altogether, he has been none the worse for the mild disease of his own creation. He considered it therefore a cruel imposition to make him give up mineral oil of which he was fond beyond its laxative effect. Breaking this habit in time, however, may have saved him from more serious and enveloping lung changes in the future.

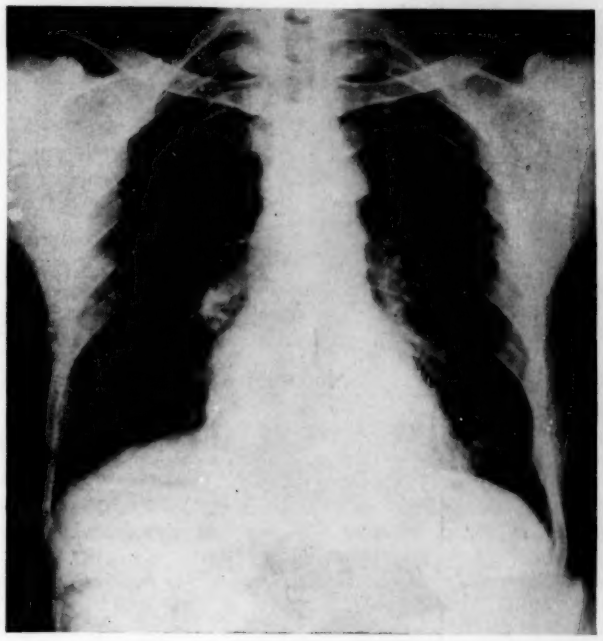

TABLE 6. *Roentgenogram Taken on August 15, 1935, in Case 5.*

CASE 5. H. C., a 60-year-old bookkeeper, was referred for bronchography because of obscure bilateral basal pulmonary lesions, more marked on the right side. He gave a history of repeated attacks of bronchopneumonia for the past 12 years. After an early one of these acute infections, a chest x-ray film on August 15, 1935, showed nothing more than heavily increased markings more prominent in the region of the left lower lobe than elsewhere (Fig. 6). Numerous serial films since then had disclosed a slowly spreading right basal lesion, which was dense in its lower aspect and fluffy as it approached the normal portion of the lung above. In addition they revealed a less pronounced, spreading, infiltrative process at the left base (Fig. 7).

In recent years the patient had noticed increasing dyspnea on exertion, some cough and expectoration and a slight obstruction to the passage of food in the upper throat. Many

radiologists and chest clinicians had seen him in the course of years, but no working diagnosis of the pulmonary lesion had been made. Bronchoscopy yielded negative results, as did sputum examinations. When he appeared for bronchography 12 years after the initial study, he gave a history of having taken mineral oil nightly in doses of about 1 ounce regularly for over 15 years. Instillation of iodized oil on July 12, 1947, showed distorted and obstructed bronchi in

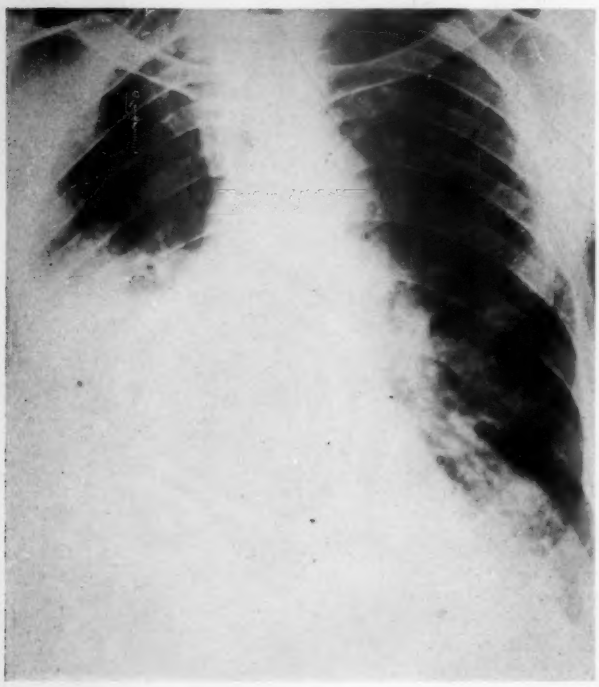

FIGURE 7. *Roentgenogram in Case 5 Taken Ten Years after That in Figure 6, Showing Upward and Conglomerate Progression of the Lesion.*

Note the very dense process on the right and the infiltrative lesion on the left.

the region of both lower-lobe granulomas and the surprising accidental finding of a Zenker diverticulum (Fig. 8).

This case is similar to the one reported by Tchertkoff,[17] which subsequently came to autopsy and showed the typical findings of mineral-oil pneumonitis. The latest films demonstrated a more extensive involvement than that in any of the other patients described above. This is accounted for in part at least by the frequently superimposed pneumonias from which the patient suffered. Unfortunately for him, the cause of the basal pulmonary disease was not established till more than a decade after he came under observation. He has now ceased taking mineral oil for a year, the chest picture has remained unaltered, and his symptoms are practically unchanged. Operative removal of the Zenker diverticulum has been contemplated. The accidental finding of this pulsion diverticulum may be attributed to the fact that the bronchogram was done by the supraglottic route rather than via catheter.

SUMMARY

A typical clinicoroentgenologic picture occurring in some ambulatory older patients who have been habitually taking mineral oil for laxative purposes is described.

The gravitational distribution of the lesions and the paucity of symptoms and physical signs, at least in the early phases of this man-made disease, are emphasized.

It appears clear that it takes some time for a roentgenologically evident pulmonary reaction to this bland, liquid foreign body to develop.

Because of the age of these patients, if the lesion due to the aspiration of liquid petrolatum is one sided, the common error is made of calling this benign disease a malignant neoplasm and subjecting the patient to needless lobectomy or pneumonectomy.

Because 3 of the 5 cases were picked up on tuberculosis case-finding surveys and because all 5 were seen within a two-year period, it is predicted that many more such cases will be discovered in older population groups if the index of suspicion of the disease remains high.

In view of this experience, a chest survey of well adults who take mineral oil for the relief of constipation is being undertaken to ascertain the extent

FIGURE 8. *Roentgenogram Taken on July 12, 1947, in Case 5, Showing Further Progression of the Lesion.*

of the pulmonary hazard to the habitual users of this bland laxative.

Since this paper was submitted for publication, 2 additional cases of oil-aspiration pneumonitis in ambulatory adults who had been taking liquid petrolatum as a laxative for many years have been encountered; one was seen in consultation because of a history of repeated episodes of low-grade lower respiratory infections, and the other, picked up on survey, had a small, circumscribed lesion (paraffinoma) at the right base diagnosed as lung tumor preoperatively.

References

1. Alexander, B., Lorenzen, E., Hoffman, R., and Garfinkel, A. Effect of ingested mineral oil on plasma carotene and vitamin A. *Proc. Soc. Exper. Biol. & Med.* **65**:275-278, 1947.
2. Editorial. Effects of mineral oil. *J. A. M. A.* **135**:512, 1947.
3. Laughlen, G. F. Studies on pneumonia following naso-pharyngeal injections of oil. *Am. J. Path.* **1**:407-414, 1925.
4. Goodwin, T. C. Lipoid cell pneumonia. *Am. J. Dis. Child.* **48**:309-326, 1934.
5. Tchertkoff, I. G., and Ornstein, G. G. Bronchopulmonary disease attributed to use of intranasal instillation of oily substances: report of ten cases. *Quart. Bull. Sea View Hosp.* **1**:139-159, 1936.
6. Freiman, D. G., Engelberg, H., and Merrit, W. H. Oil aspiration (lipoid) pneumonia in adults: clinicopathologic study of forty-seven cases. *Arch. Int. Med.* **66**:11-38, 1940.
7. Nathanson, L., Frankel, D., and Jacobi, M. Diagnosis of lipoid pneumonia by aspiration biopsy. *Arch. Int. Med.* **72**:627-634, 1943.
8. Sweeney, W. J. Intranasal medication with oils. *Eye, Ear, Nose & Throat Monthly* **22**:335-338, 1943.
9. Brown, A. L., and Biskind, G. R. Differential diagnosis between lipid pneumonia and pulmonary neoplasm: report of cases: treatment by partial lobectomy. *J. A. M. A.* **117**:4-6, 1941.
10. Sodeman, W. A., and Stuart, B. N. Lipoid pneumonia in adults. *Ann. Int. Med.* **24**:241-253, 1946.
11. Schneider, L. Chronic benign pneumonitis: its discovery in older individuals with diminished or absent gag reflex. *New York State J. Med.* **48**:520-522, 1948.
12. Corper, H. J., and Freed, H. Intratracheal injection of oils for diagnostic and therapeutic purposes. *J. A. M. A.* **79**:1739-1743, 1922.
13. Pinkerton, H. Oils and fats: their entrance into and fate in lungs of infants and children: clinical and pathologic report. *Am. J. Dis. Child.* **33**:259-285, 1927.
14. Clinico-pathologic Conference. Pulmonary disease of unknown origin. *Am. J. Med.* **4**:436-446, 1948.
15. Ikeda, K. Lipoid pneumonia of adult type (paraffinoma of lung): report of five cases. *Arch. Path.* **23**:470-492, 1937.
16. Farber, J. E., Carpenter, T., and Pellicano, V. Lipoid pneumonia: diagnosis by aspiration biopsy. *Am. Rev. Tuberc.* **45**:453-455, 1942.
17. Tchertkoff, I. F. Lipoid pneumonia in patient with diverticulum of oesophagus: report of case. *Quart. Bull., Sea View Hosp.* **7**:334-340, 1942.
18. Wood, E. H., Jr. Unusual case of carcinoma of both lungs associated with lipoid pneumonia. *Radiology* **40**:193-195, 1943.

COMPLICATIONS FOLLOWING PARAVERTEBRAL LUMBAR SYMPATHETIC BLOCK WITH NUPERCAINE IN OIL*

Report of a Case

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THE complications following the use of procaine and procaine-like compounds in producing therapeutic and diagnostic paravertebral lumbar sympathetic blocks are infrequently reported in the literature. However, the relation of the sympathetic chain to the spinal cord and the major vessels in much of its course, the relatively poorly controlled method of placing the anesthetic solution around the chain and the toxicity of the anesthetic agents used make the procedure occasionally hazardous.

Shumacker,[1] in his experiments with guinea pigs, found the *median* lethal dose of procaine (*U.S.P.*) when injected into the lumbar paravertebral area to be half the subcutaneous dose. He also reported 2 clinical cases of shock-like episodes following the use of procaine for paravertebral lumbar sympathetic block.[2] From his observations, Shumacker[2] believed that the aged tolerate local anesthetic agents less well than the young do.

Although the subarachnoid space was occasionally entered during use of the paravertebral sympathetic block before the case reported below, this has been easily recognized by the usual precautions and without ill effect. Entry into the subarachnoid space seems to be more common when the needle is directed cephalad.[3] Adelman and Irwin[4] reported 2 nonfatal cases of aseptic meningitis in young white men following paravertebral lumbar sympathetic blocks using 30 cc. of 1 per cent procaine solution in each case. The spinal fluids showed, respectively, 4000 and 3485 leukocytes, predominantly polymorphonuclears, per cubic millimeter. The spinal-fluid sugars were normal in both cases. Smears and cultures for organisms were negative. The meningitis was interpreted as being due to a chemical irritation produced by pyrogens in the distilled water of the solution used. Aseptic or chemical meningitis following spinal anesthesia was reported by Orkin[5] as occurring in 0.26 per cent of 45,966 cases collected from the reports of twenty authors. Livingstone et al.[6] described 2 cases of chemical meningitis following spinal anesthesia and also reviewed 8 other case reports of the same complication. Of the 8 cases, 2 had followed the use of nupercaine, 4 procaine only, 1 procaine and epinephrine, and 1 procaine and strychnine. In this group there were 3 deaths: 1 after nupercaine, and 2 after procaine anesthesia.

The following is a case report describing complications without recovery after a paravertebral lumbar sympathetic block using nupercaine in oil.

Case Report

N. R., an 87-year-old widower, entered the hospital on April 20, 1948. About 1 week prior to admission a small "infection" had developed over the first metatarsophalangeal joint of the right foot. Five days before admission he burned his foot with a hot bath. He gave no history of diabetes by name and symptoms.

The past history revealed occasional ankle edema for the past few years. The remainder of the history was irrelevant.

Physical examination showed a well preserved, small, alert and co-operative man who had a poor memory. The dorsum of the right foot was red, swollen and tender. At the base of the toes there was a linear, depressed, darkly crusted area measuring 5 by 2 cm. Overlying the first metatarsophalangeal joint on the right was an oval, blackish area over 0.5

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cm. in diameter. The dorsalis pedis and posterior tibial pulsations were faintly palpable bilaterally. The radial arteries were sclerotic and tortuous, with marked beading. The heart was normal except for an occasional premature systole. The chest was narrow, and a moderate dorsal kyphosis was present. The lung fields were clear to percussion and auscultation.

The temperature was 98.6°F., the pulse 84, and the respirations 20. The blood pressure was 156/88.

Examination of the blood revealed a hemoglobin of 80 per cent and a white-cell count of 8700. The urine had a specific gravity of 1.015, was free of sugar and showed a ++ reaction for albumin, and the sediment contained many white cells and a few white-cell casts. The nonprotein nitrogen was 34 mg. per 100 cc. The fasting blood sugar level was 80 mg. per 100 cc. The blood Hinton test was negative.

The patient was placed on bed rest and given intramuscular injections of penicillin. It was believed that hot wet packs to the foot and leg were indicated. After 1 day the condition of the foot seemed worse, and examination revealed that no dorsalis pedis or posterior tibial pulsations were palpable. The hot wet packs were discontinued, and moist boric dressings were instituted. The cellulitis subsided, but healing was slow. The first and second toes began to show some dark discoloration. It was decided to perform a right paravertebral lumbar block. The block was performed 5 days after entry according to the method of White and Smithwick,[7] using 40 cc. of 1 per cent procaine solution. The procedure was followed by improvement in the color and increase of temperature of the foot. Four days later a second block was performed. This time nupercaine in oil was used in an attempt to prolong the effect. A total of 10 cc. of the solution was used, containing 50 mg. of nupercaine. The improvement of the circulation to the foot was prolonged. On the 12th hospital day a third block was attempted. With the patient in the left lateral recumbent position, 20-gauge spinal needles were placed at the level of the first, second, third and fourth lumbar vertebras. There was no evidence that the subarachnoid space had been entered, aspiration at each level yielding no spinal fluid. At each site 2.5 cc. of nupercaine in oil was injected — a total of 10 cc. (50 mg. of nupercaine hydrochloride). Shortly after the injections the patient began complaining of "numbness" in both legs and then of inability to move either leg. A level of sensory anesthesia was identified just below the umbilicus. The patient was placed in the sitting position. There was no further rise in the level of the sensory anesthesia. Within a few minutes he complained of feeling faint, and he became pallid. The blood pressure dropped to 40 systolic, nearly 0 diastolic. The pulse was 90 and regular. The respirations remained slow and regular. Two minims of 0.5 per cent neosynephrin was given intravenously, with a resulting rise of the blood pressure to 220/120. Gradually the patient became somewhat stuporous, responding poorly. Nasal administration of oxygen was started. The blood pressure returned to 140/80. The pulse was 84. The blood pressure and pulse then remained stabilized. About 40 minutes after the injection of the nupercaine, the patient developed clonic movements of the upper extremities, which were relieved by the intravenous administration of 0.16 gm. of sodium phenobarbital. The clonic movements recurred after 2 hours, and another 0.064 gm. of sodium phenobarbital was given. Respirations were regular, varying between 20 and 24.

On the following day the patient remained drowsy and rather disoriented; this was thought to be largely due to the barbiturates that he had received. Motion and sensations returned to the left leg, but there was still a motor paralysis and anesthesia of the right leg. The blood pressure and pulse remained normal. The temperature rose to 101°F. Two days after the paravertebral lumbar injection the patient became quite stuporous and could be roused only by painful stimuli. The temperature rose no higher than 100°F., but the pulse ranged between 100 and 110. On the 4th day after injection the patient continued in a stuporous state. The temperature rose to 101°F. by axilla. He was maintained on intravenous fluids and had a urinary output of 2000 cc. in 24 hours. The nonprotein nitrogen on this day was 70 mg. per 100 cc. It was noted that cervical rigidity had developed and that he winced when the neck was flexed. He moved both extremities at this time. Other findings were flattening of the nasolabial fold on the right, no sensory response below the neck and absent abdominal, patellar and calcaneal tendon reflexes. The Babinski response was present bilaterally.

A lumbar puncture was performed in the third interspace. The initial spinal-fluid pressure was equivalent to less than 50 mm. of water. The fluid was cloudy yellow, had a faint odor of the nupercaine-in-oil solution (oil of sweet almond) and clotted on standing. There were 4060 white cells per cubic millimeter, of which 84 per cent were polymorphonuclear neutrophils and 16 per cent were lymphocytes. A stained smear of the fluid demonstrated no organisms. The protein content of the fluid was 800 mg. per 100 cc. Insufficient quantity of fluid was obtained to determine the sugar content. Culture demonstrated no growth on blood agar. Twenty thousand units of penicillin was injected intrathecally. One hundred thousand units of penicillin was given parenterally every 3 hours, and 5 gm. of sulfadiazine was given intravenously in 3000 cc. of fluid. The temperature rose to 104.6°F. by rectum. The respirations became labored and shallow. At 7:30 a.m. on April 5 — 4 days after the last paravertebral lumbar injection — the patient died.

Permission for autopsy was obtained, but the body was removed from the hospital prematurely and post-mortem examination was not performed.

Discussion

The agent used makes this case somewhat more complicated than those previously reported. Nupercaine in oil is dispensed in 5-cc. vials, a solution of 0.5 per cent nupercaine (25 mg.), 1 per cent phenol (50 mg.) and 10 per cent benzyl alcohol (0.5 cc.) in oil of sweet almond. This preparation is primarily prepared for use in proctologic surgery. The benzyl alcohol and phenol have antipruritic properties, and the phenol also probably aids in reducing the surface tension. Previously, no difficulty with the solution had been encountered in this hospital. One "collapse" reaction, which occurred after a lumbar block, was done with 1 per cent procaine solution in physiologic saline solution.

No reports of the results of injection of phenol into the spinal canal are available. The toxic dose, orally, is given as 8 to 15 gm.[8] Phenol is a general protoplasmic poison. In toxic amounts it is responsible for shock following widespread capillary damage. The blood pressure falls as a result of central vasomotor depression, but more because of the direct toxic action on the myocardium and finer blood vessels. Cold sweating is prominent; the urine is scanty and contains albumin and casts. Death results from respiratory failure, usually within twenty-four hours. The body temperature falls markedly. In man little central stimulation is observed, and the prominent effects are those of central depression.

The amount of phenol injected in this case would be no more than enough to act as a local anesthetic and irritant. Of the total of 10 cc. of solution used, containing 100 mg. of phenol, only a small amount probably entered the subarachnoid space. The marked fall in blood pressure that occurred responded quickly to neosynephrin, indicating no widespread injury to the capillaries or finer vessels. Sweating was not seen. Respirations remained regular until four days after the injection. The temperature

showed no change from normal until the day following injection when it became elevated. There were no marked changes in the character of the pulse, except for some increase in rate after the temperature began to rise. It seems safe to assume that the phenol played no important part in the patient's reaction.

Benzyl alcohol (phenyl carbinol) is relatively nontoxic, being rapidly converted to hippuric acid in the body.[9] It is irritating and somewhat corrosive as pure substance, but the watery solutions that contain up to 4 per cent are not. In all proportions it is soluble in oil and is somewhat antiseptic. In dogs spinal anesthesia has been produced by 2 to 4 per cent solutions in saline or oil.[10] Aqueous solutions have only brief anesthetic action, and the anesthesia produced is uncertain. It seems unlikely that, except for some possible transient anesthesia and a questionable irritation of the leptomeninges, the benzyl alcohol was responsible for any of the symptoms presented in this case.

Oil of sweet almond (*oleum amygadalae expressum*) is one of the fixed fatty oils and considered nontoxic and nonirritating.[11] Lipiodol, which is iodized poppy-seed oil containing about 40 per cent iodine in organic combination, when injected intrathecally is said to cause a well marked transitory aseptic meningitis with symptoms of meningeal irritation.[12] Boyd[13] states that degenerative changes in the gray matter and thrombosis of the vessels of the anterior horns may also occur. The oil of sweet almond may have been responsible for some of the cellular reaction seen in the spinal fluid.

Nupercaine is the most toxic of the commonly employed anesthetics, and on intravenous injection is six times as toxic as cocaine.[14] Clinical toxicity, however, seems to depend upon the concentration, and the extreme dilutions used for spinal anesthesia result in very little evidence of toxicity. The dosages for spinal anesthesia vary between 6 and 10 mg. Nupercaine is more rapidly absorbed from the subarachnoid space than from any area (except after intravenous administration).[15] The most prominent toxic effects of nupercaine are on the circulatory system and are more pronounced than those from any of the other commonly employed spinal anesthetics.[16] Bieter et al.,[17] experimenting with spinal anesthesia in rabbits, observed irritant or toxic symptoms with ocular complications, convulsions and spasticity of the head, neck and forelegs. Of the procaine and procaine-like compounds used, nupercaine and pantocaine (tetracaine hydrochloride, *U.S.P.*) showed the toxic effects most frequently. Davis and his associates,[18] using nupercaine, procaine and similar compounds intrathecally in dogs, found the most constant change to be an aseptic meningeal reaction. For the most part, the exudates were of the lymphocytic type. The authors also observed degenerative changes in the spinal cord.

In the case reported above, the initial fall of blood pressure, with the pulse remaining at near normal levels, frequently seen with spinal anesthesia, was probably the result of absorption of nupercaine from the spinal canal. The response to the sympathomimetic agent is somewhat confirmatory. Since the level of anesthesia never rose above the umbilicus and there was no evidence of respiratory paralysis, it can be assumed that the later stupor and convulsive movements of the arms were systemic reactions to the nupercaine similar to the reactions described by Shumacker.[2] Control of the clonic movements by barbiturates favors this explanation. In view of the experiments of Davis,[18] Orkin[5] and Livingston,[6] one is led to believe that the nupercaine was chiefly responsible for the meningeal reaction.

The increasing stupor and changes of respiration during the day before death probably were signs of increasing reaction.

Summary

A case is reported of an elderly man who, having shown a good peripheral vascular response to two previous paravertebral lumbar sympathetic blocks, developed motor and sensory changes, circulatory depression, stupor, convulsive movements of the upper extremities and late signs of meningeal irritation with death after a third block, using nupercaine in oil. The nupercaine seemed to be the chief causative agent, with possible added effects of the phenol, benzyl alcohol and oil of sweet almond — other ingredients of the solution used.

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References

1. Shumacker, H. B., Jr. Reactions of local anesthetic agents. I. Experimental studies with procaine. *Surgery* **10**:119-133, 1941.
2. *Idem.* Reactions to local anesthetic agents. II. Clinical report. *Surgery* **10**:134-144, 1941.
3. White, J. C. Technic of paravertebral alcohol injection: methods and safeguards in its use in treatment of angina pectoris. *Surg., Gynec. & Obst.* **71**:334-343, 1940.
4. Adelman, M. H., and Irwin, C. I. Acute aseptic meningitis following paravertebral lumbar sympathetic blocks. *Anesthesiology* **7**:422-425, 1946.
5. Orkin, L. D. Reported mortality and morbidity following spinal anesthesia. Presented at American Society of Regional Anesthesia, Scientific Session, March 3, 1936.
6. Livingstone, H. M., Wellman, V., Clark, D., and Lambros, V. S. So-called "aseptic or chemical meningitis": report of two cases. *Surg., Gynec. & Obst.* **77**:216-218, 1943.
7. White, J. C., and Smithwick, R. H. *The Autonomic Nervous System: Anatomy, physiology, and surgical application.* Second edition. 469 pp. New York: Macmillan Co., 1947. Pp. 451-454.
8. Goodman, L., and Gilman, A. *The Pharmacological Basis of Therapeutics: A textbook of pharmacology, toxicology and therapeutics for physicians and medical students.* 1383 pp. New York: Macmillan Co., 1941. P. 828.
9. *Idem.* P. 304.
10. Sollmann, T. *A Manual of Pharmacology and Its Applications to Therapeutics and Toxicology.* Fifth edition. 1190 pp. Philadelphia: W. B. Saunders Co., 1936. P. 325.
11. *Idem.* P. 128.
12. Ayer, J. B. Diseases of nervous system: important symptoms and signs. In *A Textbook of Medicine.* Edited by R. L. Cecil, W. McDermott, and H. G. Wolff. Seventh edition. 1730 pp. Philadelphia: W. B. Saunders Co., 1947. P. 1518.
13. Boyd, W. *The Pathology of Internal Diseases.* Fourth edition. 857 pp. Philadelphia: Lea & Febiger, 1944. P. 712.
14. Goodman, L. and Gilman.[8] P. 302.
15. Schlaepfer, K. Nupercaine spinal anesthesia in general surgery. *Anesth. & Analg.* **18**:334-338, 1939.
16. Bieter, R. N. Applied pharmacology of local anesthetics. *Am. J. Surg.* **34**:500-510, 1936.
17. Bieter, R. N., Cunningham, R. W., Lenz, O., and McNearney, J. J. Threshold anesthetic and lethal concentrations of certain spinal anesthetics in rabbit. *J. Pharmacol. & Exper. Therap.* **57**:221-244, 1936.
18. Davis, L., Haven, H., Givens, J. H., and Emmett, J. Effects of spinal anesthetics on spinal cord and its membranes: experimental study. *J. A. M. A.* **97**:1781-1785, 1931.

STREPTOMYCIN IN THE THERAPY OF TUBERCULOSIS OF THE ENDOMETRIUM*

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THE apparent arrest of endometrial tuberculosis consequent to treatment with streptomycin, hitherto unreported, appears to warrant the report of the following case.

CASE REPORT

C. L. (C.V.A.H. 10,137), a 26-year-old married woman, was referred to Cushing Veterans Administration Hospital by Dr. John Rock on November 20, 1947, for the treatment of tuberculous endometritis. She had been well until 1942, when she noted that her menstrual periods, which previously had lasted 4 or 5 days, were prolonged to 8 or 9 days. The flow was not excessive, and the cycle of about 30 days remained unchanged. She also began to have a white, nonodorous vaginal discharge. In April, 1944, she was married. At about this time she began to have vague cramps in both lower quadrants of the abdomen. These occurred irregularly, were not related to her periods and were not sufficiently severe to interfere with her activities. All these symptoms persisted without change until admission. In addition, during the 2 years prior to admission a vesicular rash had appeared on the shoulders at the time of her periods, and she had lost 20 pounds in weight during that time. Late in 1945 she consulted an obstetrician because of her failure to conceive. No cause was found. In July, 1947, she consulted Dr. Rock because of sterility. An endometrial biopsy revealed tuberculosis of the endometrium. A second biopsy in September was identical, and she was referred for treatment with streptomycin.

The past history was essentially noncontributory. The patient had had the usual childhood diseases and, in 1939, typhoid fever. There had been no other serious illnesses, and no operations. She had always lived in the eastern part of the United States, and until 1941 in a region where the milk was not pasteurized.

Both parents were living and well. There were no dead siblings and no family history of tuberculosis or history of exposure to it.

She had worked as an accountant prior to service in the WAVES from February, 1943, to January, 1946, and again was working as an accountant.

Physical examination showed a somewhat underdeveloped and undernourished, intelligent, co-operative woman, in no distress. The weight was 130 pounds. The temperature was 98.6°F. The head, neck, eyes and ears were not remarkable; the tonsils were present, but were not inflamed. The teeth were in good condition. The chest was symmetrical, with normal expansion, and the lungs were clear to percussion and auscultation. The abdomen was normal on inspection and palpation; the back and extremities showed no abnormalities. The reflexes were physiologic. There was no enlargement of the lymph nodes. Pelvic examination showed a normal marital introitus; the uterus was normal in size and position, the left ovary palpable but not enlarged, and the right ovary not felt; there were no masses. The cervix appeared normal; there was a moderate amount of slightly frothy yellow vaginal discharge. Rectal examination was negative.

Examination of the urine revealed a trace of albumin on one of twelve examinations but was otherwise negative. The nonprotein nitrogen was 21 mg. per 100 cc. The blood Kahn reaction was negative. The red-cell count was 4,100,000, with a hemoglobin of 11.2 gm., and the white-cell count 7900, with 52 per cent segmented neutrophils, 4 per cent band forms, 34 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophils; the red cells and platelets were normal in appearance. During the hospital course the hemoglobin ranged from 11.2 to 12.2 gm., the white-cell count between 4100 and 7900, and the hematocrit from 38 to 40 per cent.

Several smears and cultures of the vaginal discharge were negative for acid-fast bacilli; a smear for trichomonas was also negative. An audiogram before treatment was within normal limits. Three x-ray examinations of the chest showed no abnormality.

The tissue section of the endometrial biopsy taken in September was obtained. The report was as follows:

> Scattered small tubercles are found, with Langhans' giant cells present. The glands possess a few small papillary projections. The nuclei are predominantly basal. There is slight mucous production. Scattered mitotic figures are observed. There are degenerated neutrophils within the glands. Occasional groups of lymphocytes are seen in the stroma. The pathological diagnosis is tuberculosis of the endometrium.

On November 29 streptomycin therapy, consisting of 0.5 gm. intramuscularly every 12 hours, was begun. This was continued for 129 days. There were no untoward symptoms. Audiograms made at 2-week intervals and at the end of treatment showed no loss of hearing. The patient remained in bed except for 1 hour each day. Streptomycin blood levels were determined every 2 weeks. The level was consistently 32 or 64 units per cubic centimeter, except on two occasions when it was 8 and 16 units. Except for a single evening temperature of 100°F., the patient was afebrile. Eosinophil counts during treatment were 2, 2, 11, 9, 3, 3 and 3 per cent. The sedimentation rate was 19, 14 and 20 mm. per hour on three examinations.

The vaginal discharge diminished in amount. Three menstrual periods showed the prolonged flow experienced before treatment.

On March 22, 1948, pelvic examination under anesthesia was essentially the same as on admission. The uterus was normal in size and position. The cervix was dilated with ease, the cavity measuring 7 cm. deep, smooth and symmetrical. A moderate amount of normal-appearing endometrium was obtained by curettage. One strip of endometrium was used for guinea-pig injection. The animal was killed on May 13; there was no evidence of tuberculosis.

Microscopical examination of the endometrium revealed straight glands with basal nuclei. There was little production of mucus. No tubercles were found, and there was no inflammatory exudate. The diagnosis was normal endometrium, proliferative phase.

The patient was discharged on April 2 and returned on June 1. She had been well and had resumed her work. There had been two menstrual periods with normal flow of 4 or 5 days, the last one on May 14. Dilatation and curettage was performed on June 2. The findings were the same as before, the pathological report showing normal secretory endometrium, with no evidence of tuberculosis. A cervical biopsy was also negative. One piece of endometrium was used for guinea-pig injection. The animal was killed on July 15, and showed no evidence of disease.

The patient was returned to Dr. Rock for further study from the point of view of sterility. The following is a condensation of his report of a culdoscopy and insufflation done on July 24:

> The fundus is visualized over part of the posterior wall, and part of the summit, and appears normal. There are apparently no adhesions around the uterus. Both ovaries are partly adherent to the broad ligament, but otherwise appear normal. The right tube looks normal, and is seen throughout its length. It varies somewhat in thickness, but not to an unusual degree. The color varies from red to reddish yellow, but this variation is also quite commonly

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seen on culdoscopic examination. The fimbriated end looks as though it were closed by very delicate adhesions that extend outward to the broad ligament and the ovary. The left tube appears essentially the same except that the fimbria are tufted, and apparently open. There are a few adhesions leading from the fimbriated end outward to the broad ligament.

When a cannula is inserted into the uterine cavity, gas apparently does not pass at a pressure under 200 mm. of mercury; at 200 mm. there is a very slow leak somewhere, with no audible sound at the external os. Possibly, the left tube is patent at high pressure.

Discussion

This patient presented no evidence of tuberculosis other than in the endometrium. It is impossible to say that the disease did not exist elsewhere, particularly in the tubes. Pottenger[1] states that tuberculosis of the uterus is almost always secondary to tuberculosis elsewhere in the body, usually the tubes, and Norris[2] that the tubes are invariably involved, but most authors give 85 to 90 per cent as the figure.

Data in the literature on the incidence of tuberculosis of the genital tract vary remarkably. Jameson[3] gives a table of autopsy findings in women dying of pulmonary tuberculosis. Nineteen authors are quoted, and their figures vary from 1 to 30 per cent, with an average of 9 per cent involvement of the genital organs.

Eichner, Bookatz and Hirsch[4] found gynecologic tuberculosis in 32 cases when they reviewed 1600 autopsies and 38,000 surgical specimens. They did not state whether these patients had tuberculosis elsewhere except to mention a case of tuberculous meningitis and one with kidney involvement.

In association with sterility, the incidence is apparently higher. Rabau, Halbrecht and Casper[5] diagnosed tuberculous endometritis by strip curettage in 20 out of 208 sterile women, none of whom had evidence of tuberculosis elsewhere. Vogt (cited by Jameson[3]) found it in 7 per cent of 212 sterile women, and Jensen and McDonald[6] in 8 per cent of 25 sterile women. Rock,[7] at the Free Hospital for Women, Brookline, Massachusetts, observed only 12 cases in 2083 biopsies, an incidence of 0.6 per cent. It has been proved that pregnancy can occur and proceed to term in uteri that are the seat of tuberculosis, but Jameson[3] believes that the figures regarding sterility in some reported series of genital tuberculosis are not reliable (as low as 17 per cent), in that the pregnancies had probably occurred before the disease was present.

The treatment of genital tuberculosis hitherto has been primarily surgical, although there have been many proponents of x-ray therapy and other measures.

Jameson[3] reviews the various forms of treatment and cites a "salvage" of 72 per cent after radical surgery. Te Linde[8] gives the same figures for "salvage," with a primary mortality of 7 to 9 per cent and cites Greenberg as giving an 11 per cent mortality when there is tuberculous peritonitis, but 2.7 per cent when only the genital organs are involved. According to Jameson,[3] the results of medical treatment, x-ray therapy or conservative surgery are even less satisfactory.

Summary

A case of endometrial tuberculosis is presented in which the disease was apparently arrested by streptomycin therapy.

Data from the literature indicate that tuberculosis of the female reproductive organs is not an uncommon cause of sterility.

Although radical surgery is at present the treatment of choice, even when it cures the patient of the disease, it leaves her deprived of her reproductive functions, and often of her ovarian hormones.

It is suggested that further trial of streptomycin therapy in endometrial tuberculosis is warranted.

References

1. Pottenger, F. M. *Tuberculosis: A discussion of phthisiogenesis, immunology, pathologic physiology, diagnosis, and treatment.* 597 pp. St. Louis: C. V. Mosby Co., 1948.
2. Norris, C. C. *Gynecological and Obstetrical Tuberculosis.* 356 pp. New York: Appleton Co., 1921.
3. Jameson, E. M. *Gynecological and Obstetrical Tuberculosis.* 256 pp. Philadelphia: Lea & Febiger, 1935.
4. Eichner, E., Bookatz, A., and Hirsch, L. Gynecologic tuberculosis: brief review of thirty-two cases, including one of tuberculous cervicitis. *Am. J. Obst. & Gynec.* **43**:66-73, 1942.
5. Rabau, E., Halbrecht, I., and Casper, J. Endometrial tuberculosis as cause of sterility. *J. A. M. A.* **122**:801-804, 1943.
6. Jensen, R. M., and McDonald. J. R. Endometrium in tuberculous peritonitis and in sterility. *Am. J. Obst. & Gynec.* **41**:268-274, 1941.
7. Rock, J. Personal communication.
8. Te Linde, R. W. *Operative Gynecology.* 751 pp. Philadelphia: J. B. Lippincott Co., 1946.

MEDICAL PROGRESS

DERMATOLOGY

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THE tremendous volume of papers on dermatology makes it impossible for the busy specialist to keep abreast of the literature. However, the establishment of the *International Abstract*, the *Quarterly Review of Dermatology and Syphilology* and the old favorite — the *Year Book of Dermatology and Syphilology* — lighten the burden. Many reports are repetitious; others are valueless. These reviews represent an attempt to separate the wheat from the chaff.

An excellent presentation of the skin manifestations of systemic disease has been written by Wiener,[1] who has coined the word "dermadrome" for such phenomena. The discovery of a systemic disease from a clue given by cutaneous lesions is very satisfying if the discovery prevents further extension of the disease; for example, the formation of small dark warty growths on the skin may lead to the early diagnosis of an operable intra-abdominal cancer, or bluish discoloration of the skin about the umbilicus may indicate rupture with an ectopic pregnancy.

In a study of the relation of acidity of the scalp to seborrhea, Cornbleet and Bergeim[2] found that the pH varied from 4.5 to 5.5, the acidity being chiefly due to lactic acid of sweat. Volatile acids were thought to be formed by the action of organisms on the lactic acid. These acids are believed to inhibit the growth of many micro-organisms and to cause itching when concentrated.

According to Lobitz and Mason,[3] the palmar sweat glands, like the kidneys, seem able to form ammonia. Fifty-five specimens of sweat were collected from 5 normal men and 5 normal women and grouped in two physiologic types: profuse, 27 specimens, and intermittent, 28 specimens. Tests showed that the profuse palmar sweat had a lower concentration of ammonia nitrogen than the intermittent palmar sweat (7.7 and 28.9 mean, per 100 cc. respectively).

In a comparison of sweat-gland response to direct heating and to reflex stimulation, Randall[4] found that heat elicited profuse sweating by some glands, but the diffuse sweating that characterizes a reflex response was absent. There appears to be a threshold temperature, above which a direct response to local heat may occur and below which it does not occur. This critical temperature is several degrees above that necessary to induce sweating by reflex, when heat is applied to a large area. Randall concludes that the profuse sweating response of individual glands to extreme temperatures is a direct one in contrast to the usual diffuse reflex response.

GENETICS

Whittle[5] reports 2 cases of congenital poikiloderma, one in a twelve-year-old boy and the other in a four-year-old girl. There were areas of discoloration of the skin since birth, on the face, upper and lower extremities in one case and only on the cheeks in the other.

Acrokeratosis verruciformis (Hopf), a discrete keratoderma of the extremities, has a definite hereditary factor, as shown by Niedelman,[6] who reports 4 males and 10 females of one family affected with this disease. Three males and 3 females in the same family were unaffected. This disease is differentiated from epidermodysplasia verruciformis, characterized by different types of verrucous lesions, by the fact that the histologic study reveals vacuolated cells in the latter. Niedelman questions whether this is sufficient to justify considering the diseases as different entities. He believes acrokeratosis verruciformis to be a hereditary nevoid dermatosis, possibly resulting from an inherited metabolic disturbance affecting normal utilization of vitamin A.

Porter et al.[7] report 7 cases of Darier's disease (keratosis follicularis) in which 30,000 to 100,000 units of vitamin A were given daily for one to thirty months. There was great clinical improvement in 1 case, much improvement in another, little in 3 and no improvement in 2.

Hypertrichosis is frequently inherited. Reporting on electrolysis versus high-frequency currents in the treatment of hypertrichosis, Ellis[8] states that electrolysis is slower but has less recurrences and rarely causes abscesses. Although the short-wave method is rapid, it has more recurrences and frequently causes abscesses and larger scars. Histologic study showed more severe damage to the epidermis resulted from diathermy, and most hairs recurred unless visible burns were produced, leaving scars. Destruction of the individual hairs either by electrolysis or high-frequency current is the only safe method of removing hair. I prefer electrolysis.

ENDOCRINES

Watson and Pearce[9] chemically analyzed and tested against hyaluronidase biopsy specimens from 2 cases of pretibial myxedema and found that they

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contained mucopolysaccharides. The latter showed marked hydrolysis when exposed to hyaluronidase, indicating that they were hyaluronic acid. This suggests that pretibial myxedema results from a local disturbance of metabolism of mucopolysaccharides. These authors conclude that the presence of hyaluronidase in the normal thyroid gland and the recent discovery of an enzyme in the blood that destroys hyaluronidase furnish a basis for much speculation regarding the etiology of pretibial myxedema.

Ayres and Jensen[10] report complete cure of the syndrome of otorhinophyma, pruritus and alopecia totalis with testosterone by mouth, 10 mg. every one or two days for four months. The patient, a sixty-six-year-old man, had alopecia for fifteen years and later developed a generalized pruritic eruption, with inflammatory hypertrophy of the nose, ears, chin, cheeks and eyebrows, and with dystrophic nails.

After a careful study of the effect of x-ray therapy on rabbit testes, Callaway et al.[11] conclude that scattered irradiation reaching the gonadal region of the patient receiving low-voltage therapy to the face or other more remote areas is negligible so far as injury to gonadal tissues is concerned.

Ephynal, a synthetic racemic alpha tocopheryl acetate, has been recommended for pruritus due to estrogen imbalance.[12]

Reporting on the spontaneous cure of tinea capitis in puberty, Rothman[13] proves what has previously been only a theory. He shows that the reason for spontaneous cure in puberty and for adults' immunity to *Microsporum audouini* infections is that with the onset of puberty the sebaceous glands of the scalp start to secrete a sebum that contains, in higher concentration than before, low-boiling saturated fatty acids with selective fungistatic and fungicidal action on *M. audouini*. He demonstrates and identifies the low-boiling saturated fatty acids and the normal aliphatic monobasic acids with odd numbers of carbon atoms. The active fatty acids constitute a very small part of the total fat extracted, but such active acids have a minimum fungistatic concentration of 0.0005 per cent. These cures are effected slowly by the sterilization of the follicular canals and the surface of the scalp, preventing further spread, so that as the infected hairs are shed the infection disappears. This article is the result and report of a logical theory, which was tested by exact chemical procedures. Both the experiment and the article describing it are excellent.

The undermining of acne lesions by exteriorization is described by Bereston and Benteen.[14] Treatment consists of excision of the acneform area overlying the cyst or sinus beneath; healing is by granulation and occasionally grafting is indicated. The scarring of the surgical procedure is apt to be extremely disfiguring.

Dermatitis and Allergy

Klasson[15] reports a study of ascorbic acid in the treatment of poison-oak dermatitis. He believes that vitamin C is capable of preventing and combating the disease. The best results were obtained for the most part in patients with edema of the eyelids and genitalia. This theory certainly needs substantiation. If verified, it would be a boon to outdoor workers.

Epstein[16] adds another theory for the cause of localized bullous dermatitis or benign localized pemphigus — namely, focal infection. Such infection may be a factor in other cutaneous disturbances.

According to Steiner and Fishburn[17] cutaneous eruptions from streptomycin occurred in 18.2 per cent of 33 patients, a marked contrast to 4.9 per cent of 1000 cases reported by Keefer. The temptation is strong to compare these reactions with "ninth-day erythema." Steiner comments that eosinophilia and "accelerated reaction time" on readministration of streptomycin point to the allergic nature of the reactions.

Dermatitis venenata due to streptomycin is frequently seen in nurses administering the drug.[18]

Zakon et al.[19] report 32 cases of lipstick cheilitis due to a bromfluorescein dye. All were cured by the substitution of lipsticks that contained no halogen derivative of fluorescein.

Discussing the treatment of diaper rash, Benson et al.[20] recommend diapene (manufactured by Homemakers' Products Corporation), a quarternary ammonium compound (para di-isobutylcresoxy-ethoxy-ethyl di-methyl benzyl ammonium chloride monohydrate). Diaper rash is thought to be an ammonia dermatitis caused by decomposition of urea to free ammonia by *B. ammoniagenes* in the feces. Diapene inhibits *B. ammoniagenes* in vitro in dilutions of 1:200,000. Patch tests with 1:5000 dilution elicited no reactions. Of 50 cases treated, 49 were cured in a week; 1 case did not respond. There were 14 recurrences in two weeks after discontinuance of diapene, with a rapid response when it was used as a diaper rinse. These diapers should be a blessing to tired mothers. Diaper rash is a frequent occurrence and often resistant to treatment.

Robertson[21] believes that the emotional background of a dermatitis may cause an acute exacerbation, and even resentment on the part of the patient. He presents a keen analysis of the patient's problems and the proper approach in directing their solution.

Forman[22] reports that evipan narcosis offers a quick and probably reliable method of psychologic investigation that may be of value to the dermatologist for study on the basis of neurogenic cutaneous diseases.

Owing to the ease of application, a new device, zippered elastic stockings, should be of value in the treatment of stasis dermatitides.[23]

Pfeiffer and Williams[24] think that a suspension of paraldehyde is a valuable sedative for patients suffering from pruritus. Its taste being obnoxious, it is disguised in the following prescription:

Substance	Amount
Paraldehyde (*U.S.P.*)	50
Powdered gum tragacanth	2
Glycyrrhiza syrup (as needed)	120

Make a suspension; shake before using 4 cc. in ice water.

Combes[25] recommends a new tar preparation, zetar, but does not give its composition. Pure coal tar direct from the gasworks is an inexpensive and efficient preparation for the treatment of persistent cutaneous diseases. No matter how its derivative is incorporated in a compound, it helps a given number of patients, but sensitizes others.

Sharlit[26] does not believe that the alkalinity of toilet soap is dangerous for the skin. Nineteen samples of face powders bought at random were suspended overnight in water and the pH determined; all were on the alkaline side. He states that the fact that frequently used alkaline face powders do not cause damage to the face suggests that the damage from toilet soaps is exaggerated. He apparently disregards the difference in the methods of applying these substances.

Ellis[27] has reported 9 cases of allergic contact dermatitis due to wool fat and cholesterol.

By patch tests Lane and Blank[28] found that fatty acids of low molecular weight (lauric and oleic) were more irritating than those of high molecular weight. Among fatty acids present in soap in appreciable amounts, lauric and oleic acid gave more positive reactions. Patch tests of patients with chronic recurrent vesicular eruptions of the hands confirmed the foregoing observations. The authors state that sulfated oleic acid depends on the degree of sulfation for its irritation of the skin. If highly sulfated and combined with palmitic and stearic acids in a soap (dermolate), it is practically nonirritating.

I have followed with great interest the progress of the appearance of synthetic detergents during the last decade. The recent war, with its attendant shortages, gave them a tremendous impetus. The literature has been most misleading. Industrialists have installed expensive receptacles to supply these so-called nonirritant soap substitutes to the workers. Patients with erupted skins have been advised that they can use the detergents with impunity. It is my opinion that they are of little or no value and are much overrated, being promoted, as some brands of cigarettes are, through a few well chosen papers by nonmedical research workers supported by grants given to large clinics. I have tested them on normal and diseased skins and found them wanting. I prefer the soaps from natural oils for normal skins and soothing vegetable oils for inflamed skins.

Apparently there will always be a skin perverse enough to do the unexpected — for example, to become sensitized to an anti-histamine drug. A case is reported of an eczematoid dermatitis of the hands, chest and thighs appearing after the use of pyribenzamine to prevent recurrent colds. With cessation of the dermatitis, repetition of ingestion of the drug caused a recurrence.[29] This type of reaction challenges the histamine-release theory of allergic dermatoses.

Lowell[30] states that the understanding of allergic reactions remains incomplete. The difficulty lies in the absence of a direct means of investigating the conditions. Apparently it is the cell itself that is sensitized, and this is why these drugs have been of so little value in contact dermatitides.

Whittemore and DeGora[31] report a successful passive transfer to sulfadiazine twenty-five days after an acute episode. Ten minutes after a dose of 0.5 gm. of the drug (which had been taken a month previously for treatment of furunculosis), the patient had a cutaneous reaction consisting of itching, flushing and large wheals.

Frazier and Small[32] present a thorough consideration of the immunologic and biochemical implications of allergic dermatitis. Their rational and inquiring discussion covers the question whether drug reactions are due to sensitization or toxicity and operate directly or by tissue combination. The authors believe that the disturbance in lipid metabolism that occurs in this disease should be investigated.

Aminophyllin (0.5 gm. in 2.0 cc. of fluid given intramuscularly) was tried by Epstein[33] in 17 cases of pruritic eruptions. Seven patients had dramatic relief in three to forty-five minutes, with no recurrence for twelve to thirty-six hours. One patient with eczema obtained relief for six days. Two patients were relieved, and subsequent injections controlled recurrences. Three patients with eczema, 2 with generalized pruritus and 1 with urticaria experienced no relief. Three patients obtained mild benefit, and 1 failed to return. It was noted that the local and general reactions were too severe for general use of this drug as an antipruritic agent. The injections require care in preparation, are very painful, with soreness persisting for days, and cause nausea. One patient nearly died from shock, and another menstruated for fifteen minutes after each of six injections. In this therapy, the cure is worse than the disease.

Loew[34] states that the major action of antihistamine drugs is probably exerted directly on the peripheral effector cells that respond to histamine, since antagonism has frequently been

demonstrated on isolated tissue or organs. The antagonism exerted peripherally could be modified by nervous or humoral influences in the intact animal.

A study was made of comparative anti-histaminic activity of six compounds by Winter.[35] He found that neoantergen caused fewer side reactions and that it was less toxic per effective dose than the other five compounds. Pyribenzamine was second in these qualities. Although these findings are claimed to be essentially in agreement with those of some investigators, they are at variance with others. Time will be required for proper evaluation of all these anti-histaminic drugs.

Halpern[36] did some experimental research on anti-histaminic drugs, thiodipharylamine derivatives. Two derivatives designated "3015 R.P." and "3277 R.P." were reported to be less toxic and more active than the best previous anti-histaminic drug discovered by the French ("antergan").

Giving a detailed report on derivatives of N, N-dimethyl-N¹2-pyridyl-ethylenediamine as anti-histaminics, Litchfield and Adams[37] state that the substance was halogenated, producing two products tentatively named "chlorathen" and "bromathen," each of which is weight for weight twice as active and half as toxic acutely as pyribenzamine. Furthermore, it was noted that equal weights of either of these substances protect twice as long as pyribenzamine.

Henderson and Rose[38] report 64 per cent improvement in 138 allergic patients treated with pyribenzamine. Side effects in order of frequency were sleepiness, nervousness, nausea, dry mouth, vertigo, insomnia, headache and vomiting. Only 2 patients required discontinuance of the drug because of reactions. Pyribenzamine has been given for as long as a year without toxic effects. Its action, as well as that of benadryl, is temporary, and therefore a thorough search for the cause of allergy and its treatment remains necessary.

Urticaria due to sunlight is a distressing ailment. Ehrlich[39] showed by selective infiltration that the wave lengths of the offending rays lie between 3000 and 3750 Angström units. The patient was a thirty-five-year-old woman who for ten years had had urticaria on the areas exposed to sunlight. It is doubtful whether the positive transfer test in these cases is due to transfer of reagins (genuine allergy) or to a photosensitizing substance (a photodynamic phenomenon). Photosensitivity to sunlight from the use of sulfonamides is still an interesting problem. Watkinson and Hillis[40] report a study of a group of 470 soldiers receiving 2 gm. of sulfanilamide daily for ten days as prophylaxis against epidemics of streptococcal sore throat. Vaccination for smallpox was given at the same time. Of 213 men receiving sulfanilamide after vaccination for smallpox, 49 per cent became photosensitive in one to ten days. These authors conclude that the results support the hypothesis that drug reactions are due to liberation of toxins from a buried toxin focus; in these cases it was the vaccination with pustular stage that supplied the toxin.

Bradley[41] reports a fatal case of periarteritis nodosa in a ten-year-old boy. The fact that this patient had had sulfonamides for otitis media at six years of age and was probably given the drug for three weeks prior to admission raises the question in her mind of the part played by sulfonamides and other drugs in the etiology of these diseases.

Rich and Gregory[42] state that it is of interest that disseminated lupus erythematosus shows "sclerotic" coronary lesions of the same type as occur in rheumatic fever and periarteritis nodosa and in animals subjected to experimental serum sickness. These lesions, they state, must be related to lupus erythematosus, since they occur in children with that disease. Their work is well organized and controlled, and several good photographs support the statements.

In a report on erythema nodosum, Favour and Sosman[43] state that the concurrence of rheumatic fever and erythema nodosum is coincidental. However, both may be theoretically considered as hypersensitivity diseases. The multiplicity of unrelated infections and drugs known to initiate erythema nodosum has tended to obscure the role of the beta-hemolytic streptococcus. They state that mild secondary anemia, cervical adenopathy and occasionally enlarged hilar or bronchial lymph nodes characterized the illness; individual predisposition, a variety of infections and chemical agents and local trauma contributed to its occurrence.

Naide[44] gives an interesting discussion of allergic lesions following thrombophlebitis. Venous thrombosis may cause trapping of an allergen to bring out a subclinical allergic state or to accentuate a pre-existing allergic lesion; stasis dermatitis or eczema results. Trauma causes outpouring of these concentrated allergens into the area as demonstrated experimentally in a sensitized rabbit in which the traumatized ear became gangrenous after injection of the allergen, the noninjured ear being unaffected. This creates a vicious circle that causes chronic ulcers. Naide concludes by warning against the use of sensitizing drugs or even adhesive tape in these areas of stasis. Sensitizing drugs such as benzocaine, nupercaine, penicillin, mercury, resorcin and the nitrofurans should not be used in the treatment of a stasis dermatitis or eczema.

Reporting on intradermal tests with dirofilaria immitis extract in human filariasis, Zeligs[45] states that the test is of some value but that it cannot be depended on exclusively. It gives too many false-positive and false-negative readings to be dependable.

Young and Yeager[46] report 2 interesting cases of cyanosis secondary to the wearing of ink-stained athletic shirts. Two students practicing football

wore sweaters heavily numbered with Sanford's indelible ink, containing carbon black, phenol, ammonia, nigrozene and aniline oil. They developed generalized cyanosis with nervousness, vertigo and dyspnea, the symptoms subsiding in approximately twelve hours. In conclusion the authors state that indelible ink containing aniline oil will produce methemoglobinemia if allowed to remain in contact with the skin for a sufficient time.

A severe delayed reaction to penicillin is reported by Dolan.[47] The patient, a twenty-six-year-old man, gave a history of treatment with penicillin intramuscularly three years and two months previously. The ear canal was treated with penicillin, both orally and locally. Three days after treatment generalized pruritus and raised, erythematous areas, 1 to 6 cm. in diameter, developed. Three days later the condition progressed to frank edema about the face and scalp, pitting edema of the ankles and feet, soreness of the buccal mucous membranes and pains in the muscles of the abdomen, back and extremities, with a temperature of 100.2°F.

Hopkins and Lawrence[48] state that sensitization from the local application of penicillin is not sufficient to prevent its subsequent parenteral use. They found sensitization severe enough to prevent or prohibit systemic treatment in less than 1 per cent of the cases.

Templeton et al.[49] state that penicillin contains two antigens — penicillin and its culture medium. Types of dermal reactions have been toxic, macular or scarlatiniform, occurring in the first few days after penicillin therapy was started, urticaria (most frequent and occurring seven to nine days after penicillin) and erythema multiforme and nodosum, bullous and lichenoid, which may occur a few hours after penicillin injection. Circulating antibodies were believed to occur on the basis of a modified Prausnitz–Küstner reaction.

According to Kiel,[50] pyoderma gangrenosum (ulceroneurotic skin lesions) and possibly the associated ulcerative colitis may be allergic reactions to bacterial infection elsewhere. She reports the case of a thirty-eight-year-old woman with an acute to chronic colitis of three years' duration, who suddenly developed many rapidly spreading, roughly symmetrical ulcers on the extremities and torso, with fever, hypoproteinemia and bone-marrow depression.

When gold compounds were injected in lethal doses into rats, BAL increased the survival time for all compounds studied — gold sodium thiosulfate, thioglucose and sodium succimidoaurate — with the exception of gold sodium thiomalate.[51] In 2 cases observed BAL produced rapid amelioration of the acute signs of a dermatitis due to gold, but final healing of the eruption followed the usual course of a slow return of the skin to normalcy.

Application of the following prescription prior to exposure was successful in the prevention of mustard-gas burns[52]:

Substance	Amount
Glycerol	50
Chloramine-T	18
Zinc oxide	50

Aldrich[53] treated 54 cases of pruritus ani and vulvae with undecylenic acid (2 per cent) in triethanolamine and zinc stearate in a water-miscible base — an emulsion. Fifty (88 per cent) were cured — that is, with no recurrences to the time of his report — in four to thirty-three days by the local application of this emulsion. Four cases were complete failures. Any such report needs confirmation. My experience in the treatment of pruritus ani and vulvae is at times disheartening.

Occupational Diseases

Benedek[54] presents a differentiation between pompholyx and occupational dermatitis to remove confusion regarding the diagnosis and treatment of the latter. He claims that in 1925 he discovered *Bacillus endoparasiticus* to be the cause of pompholyx, and that this organism is constantly harbored in a location as yet unknown, frequently in the blood. It is his contention that if one gets a contact dermatitis at this time, the organism causes pompholyx in the injured skin, and cure is difficult or impossible without the use of an anti-endoparasiticus vaccine. His ideas are in conflict with the present generally accepted concepts.

Hanzlik[55] studied the epidermal application of diethylene glycol monoethyl ether (carbitol). Carbitol and other glycols were rubbed on the skin of rabbits, in aqueous form or in ointment bases. Renal and liver damage (necrosis) were observed with toxic dosage, and this led to death. The order of toxicity was as follows: diethylene glycol was more toxic than ethylene glycol; technical carbitol, ethylene glycol and propylene glycol were more toxic than carbitol; and the LD_{50} of carbitol was 0.32 cc. to 0.08 cc. per kilogram of body weight daily. The safe dosage is probably 0.04 to 0.02 cc. per kilogram of body weight a day. Hanzlik's paper is a thorough investigation of a cosmetic and its industrial preparation. According to the Pure Food and Drug Administration, "any amount in excess of 5 per cent in preparations for topical application to small areas of the body would constitute a hazard." This study is of extreme value because of the use of carbitol and glycol in the formulas of various solutions and ointments containing medication. This toxicity must be considered when large amounts are used in large ulcers and sinuses over a long period.

Occupational cutaneous cancer in England is discussed by Henry[56] in a detailed statistical report that describes the nature of the cancer's beginning, sites of predilection and progress. Workmen's compensation for epitheliomas in chimneysweeps or workers in pitch, tar or tarry compounds was first allowed in 1907. In 1914 it was enlarged to include cancer from mineral oil, bitumen and paraffin or their derivatives. Cancer resulting from arsenic has been a notifiable disease since 1896.

Schwartz[57] describes occupational pigmentary changes in the skin. They consist of excess of melanin and melanoid, metallic substances deposited in the skin (tattooing) and staining from external or ingested dye. Occupational causes of unusual formation of pigment in the skin are excessive exposures to actinic rays, coal tar, crude petroleum and residues of distillation, and asphalt. The last three are photosensitizers. Depigmentation results from injuries, from skin infections and from monobenzyl ether of hydroquinone, the antioxidant in rubber manufacture. The last is the only chemical reported to have caused occupational depigmentation without causing dermatitis. The action is not entirely clear.

According to Klauder and Brill,[58] the irritant action of petroleum solvents, like the defatting action, decreases as the boiling range increases. Petroleum solvents with boiling ranges up to and including that of kerosene are primary irritants. Beyond kerosene there is varying reaction from none to positive. In this report Negroes had the highest tolerance. Patients with dermatoses due to petroleum solvents had less tolerance than patients with those from other causes. Naphthenic kerosene gave more severe reactions than paraffinic kerosene of the same boiling point. Klauder and Brill conclude that petroleum-solvent dermatitis is a nonspecific sensitivity.

Metabolism

In a paper on acne rosacea, Tulipan[59] states that telangiectasia, erythema, papules, pustules and hypertrophy are probably due to a deficiency of vitamin B complex, as a result of lack of intake or by faulty absorption. He cites a series of 96 cases whose response to treatment indicated that this deficiency is the primary cause of rosacea. Local treatment included an antiseptic and the following hydrophilic ointment:

Substance	Amount
Red oxide of mercury	0.075
Sulfur precipitate	1.5
Salicylic acid	1.0
"Quinolor compound ointment"	2.0
Aquaphor (as needed)	30.0

In my experience, local therapy with antiseptic compounds is a necessary adjunct to the internal treatment of rosacea. Endocrine therapy in women seems to be of value.

Sachs et al.[60] give a brief but clear presentation of their ideas on a confusing dermatologic entity frequently mistaken for dermatophytosis, even by dermatologists. They suggest the name "acrodermatitis pustulosa perstans." Their report of 11 cases states that the eruption clinically may be identical with pustular bacteride or pustular psoriasis. It persists for years and seldom remits entirely, beginning as a vesicle or pustule (sterile) on the palms, digits or soles, with predilection for the thenar portion of the palms and the center of the soles extending to the inner side of the feet. Treatment generally is ineffective. Occasionally, removal of a focus of infection or the internal administration of arsenic produces a cure.

Caro and Senear[61] consider a nonpustular psoriasis of the hands (with or without psoriasis elsewhere) to be more frequent than is generally believed. These lesions, usually seen on the extensors of the finger joints and knuckles, sides of the fingers, palms and fingertips, are bilateral but not always symmetric. A biopsy is often necessary for diagnosis. These cases are frequently mistaken for occupational eruptions.

Brunsting and Mason[62] report further studies on porphyria, stating that pigmentation occurs in the acute form but that other cutaneous reactions are rare. In congenital porphyria, however, there is marked sensitivity to light, and in the chronic disease there are bullous eruptions after light exposure and the skin reacts to trauma in a manner similar to epidermolysis bullosa.

Dunsky et al.[63] report a normal-appearing newborn baby who at two months began to pass red urine. This continued, and the patient presented loss of fingernails and bullous lesions of the hand that resisted treatment, healing with pigmented scars. The teeth were purple brown, and there was pronounced generalized hypertrichosis. Splenomegaly occurred, and the skin became more fragile. The authors include a thorough report of the chemical study of the porphyrins.

Eosinophilic granuloma, despite its rarity, is still a popular subject for theoretical discussion. Thannhauser[64] believes that this entity is only a stage in a large syndrome, which might be entitled eosinophilic xanthomatous granuloma.

In a discussion of the syndrome of "burning feet" as a manifestation of nutritional deficiency, Glusman[65] states that burning feet were first described and attributed to dietary deficiency by the British in Burma in 1826. American prisoners in the Philippines from 1942 to 1945 were afflicted by the thousands, with or without other symptoms. The first symptoms were numbness, tingling and burning of the toes and soles. Later there were sharp shooting pains in the legs, usually bilateral and worse at night. In some severe cases there was

involvement of the palms. Many patients had pellagra rashes, scrotal dermatitis, fissuring at the angles of the mouth, edema, diarrhea and so forth. These responded to nicotinic acid and riboflavin or B complex, whereas the burning feet persisted.

Lloyd and Williams[66] report a study of endocrine function in 71 patients with cirrhosis of the liver. Clinical endocrine changes observed in male patients consisted of decreased libido and potency, atrophy of the testicles, decreased body hair and gynecomastia. Telangiectasia and "liver palms" were also regarded as possibly being related to altered endocrine function. Decreased axillary hair was present in 46 of the 55 male patients (84 per cent).

An editorial in the *Journal of the American Medical Association*[67] states that "until clinical studies have been reported and critically analyzed, the local use of amino acids to accelerate wound healing can be considered only as an interesting observation."

(To be concluded)

References

1. Wiener, K. *Skin Manifestations of Internal Disorders.* 690 pp. St. Louis: C. V. Mosby Co., 1947.
2. Cornbleet, T., and Bergeim, O. Acidity of scalp. *Arch. Dermat. & Syph.* **56**:448-451, 1947.
3. Lobitz, W. C., Jr., and Mason, H. L. Chemistry of palmar sweat: ammonia nitrogen. *Arch. Dermat. & Syph.* **57**:69-73, 1948.
4. Randall, W. C. Local sweat gland activity due to direct effects of radiant heat. *Am. J. Physiol.* **150**:365-371, 1947.
5. Whittle, C. H. Poikiloderma congenitale (Thomson): two cases. *Proc. Roy. Soc. Med.* **40**:499, 1947.
6. Niedelman, M. L. Acrokeratosis verruciformis (Hopf): hereditary features. *Arch. Dermat. & Syph.* **56**:48-63, 1947.
7. Porter, A. D., Godding, E. W., and Brunauer, S. R. Vitamin A in Darier's disease. *Arch. Dermat. & Syph.* **56**:306-316, 1947.
8. Ellis, F. A. Electrolysis versus high frequency currents in treatment of hypertrichosis: comparative histologic and clinical study. *Arch. Dermat. & Syph.* **56**:291-305, 1947.
9. Watson, E. M., and Pearce, R. H. Mucopolysaccharide content of skin in localized (pretibial) myxedema. *Am. J. Clin. Path.* **17**: 507-512, 1947.
10. Ayres, S., and Jensen, A. K. Otorhinophyma, pruritus and alopecia totalis syndrome. *Arch. Dermat. & Syph.* **56**:379-393, 1947.
11. Callaway, J. L., Mosley, V., and Barefoot, S. W. Effect of roentgen ray irradiation on testes of rabbits. *Arch. Dermat. & Syph.* **56**:471-479, 1947.
12. Ephynal. *Quart. J. Pharm. & Pharmacol.* **19**:584, 1946.
13. Rothman, S., Smiljanic, A., Shapiro, A. L., and Weitkamp, A. W. Spontaneous cure of tinea capitis in puberty. *J. Invest. Dermat.* **8**:81-98, 1947.
14. Bereston, E. S., and Benteen, H. Undermining acne lesions — treatment by exteriorization. *Arch. Dermat. & Syph.* **56**:7-12, 1947.
15. Klasson, D. H. Ascorbic acid in treatment and prevention of poison oak dermatitis. *Arch. Dermat. & Syph.* **56**:864-867, 1947.
16. Epstein, S. Persistent localized bullous eruption associated with focal infection. *Arch. Dermat. & Syph.* **56**:452-458, 1947.
17. Steiner, K., and Fishburn, G. W. Cutaneous eruptions from streptomycin. *Arch. Dermat. & Syph.* **56**:511-516, 1947.
18. Canizares, O., and Shatin, H. Dermatitis venenata due to streptomycin. *Arch. Dermat. & Syph.* **56**:676, 1947.
19. Zakon, S. J., Goldberg, A. L., and Kahn, J. B. Lipstick cheilitis. *Arch. Dermat. & Syph.* **56**:499-505, 1947.
20. Benson, F. A., Slobody, L. B., Lillich, L., Maffia, A., and Sullivan, N. New treatment for diaper rash: preliminary report. *J. Pediat.* **31**: 369-374, 1947.
21. Robertson, G. G. Emotional aspects of skin disease. *Lancet* **2**:124-127, 1947.
22. Forman, L. "Evipan" used in investigation of chronic dermatoses. *M. J. Australia* **2**:340, 1947.
23. Cogswell, H. D. Zippered elastic stockings. *Surgery* **22**:993, 1947.
24. Pfeiffer, C. C., and Williams, H. L. Suspension of paraldehyde. *J. A. Pharmac. A.* **8**:572, 1947.
25. Combes, F. C. Coal tar in dermatology: improvement in its physical properties without any change in its therapeutic action. *Arch. Dermat. & Syph.* **56**:583-588, 1947.
26. Sharlit, H. Cosmetic dermatology: alkalinity of face powder mixtures. *Arch. Dermat. & Syph.* **56**:666-668, 1947.
27. Ellis, F. A. Allergic contact dermatitis due to wool fat and cholesterol. *Arch. Dermat. & Syph.* **56**:801-806, 1947.
28. Lane, C. G., and Blank, I. H. Action of soap containing little or no lauric or oleic acid. *Arch. Dermat. & Syph.* **56**:419-424, 1947.
29. Harris, M. C., and Shure, N. Eczematoid dermatitis following ingestion of "pyribenzamine hydrochloride." *J. Allergy* **18**:408-412, 1947.
30. Lowell, F. C. Newer concepts of allergy to drugs and bacteria. *J. A. M. A.* **136**:665-668, 1948.
31. Whittemore, A. L., and DeGora, P. F. Sulfadiazine sensitivity: unusual case with successful passive transfer. *J. Allergy* **18**:382-384, 1947.
32. Frazier, C. N., and Small, A. A. Allergic dermatitis: view of its immunologic and biochemical implications. *Am. J. Med.* **3**:571-585, 1947.
33. Epstein, E. Aminophylline as antipruritic agent: intramuscular injection. *Arch. Dermat. & Syph.* **56**:373-375, 1947.
34. Loew, E. R. Pharmacology of antihistamine compounds. *Physiol. Rev.* **27**:542-573, 1947.
35. Winter, C. A. Study of comparative antihistaminic activity of six compounds. *J. Pharmacol. & Exper. Therap.* **90**:224-232, 1947.
36. Halpern, B. N. Experimental research on new series of chemical substances with powerful antihistaminic activity: thiodipharylamine derivatives. *J. Allergy* **18**:263-272, 1947.
37. Litchfield, J. T., Jr., and Adams, M. R. 5-halo-2-thenyl derivatives of N, N-dimethyl-N'-2-pyridyl-ethylenediamine as antihistaminics. *Bull. Johns Hopkins Hosp.* **81**:55-64, 1947.
38. Henderson, A. T., and Rose, B. Pyribenzamine (n-pyridyl, n-benzyl, dimethyl-ethylendiaminehydrochloride) in treatment of allergy. *Canad. M. A. J.* **57**:136-140, 1947.
39. Ehrlich, E. E. Light urticaria. *Ann. Allergy* **5**:478-487, 1947.
40. Watkinson, G., and Hillis, B. H. Photosensitivity to sunlight from use of prophylactic sulphonamides: its relation to vaccination reactions. *Brit. M. J.* **2**:609-611, 1947.
41. Bradley, E. J. Periarteritis nodosa in childhood. *J. Pediat.* **31**:78-81, 1947.
42. Rich, A. R., and Gregory, J. E. Anaphylactic lesions of coronary arteries "sclerotic" type, commonly associated with rheumatic fever and disseminated lupus erythematosus. *Bull. Johns Hopkins Hosp.* **81**:312-324, 1947.
43. Favour, C. B., and Sosman, M. C. Erythema nodosum. *Arch. Int. Med.* **80**:435-453, 1947.
44. Naide, M. Allergic lesions following thrombophlebitis. *Arch. Int. Med.* **80**:388-396, 1947.
45. Zeligs, M. Intradermal tests with *Dirofilaria immitis* extract in human filariasis. *U. S. Nav. M. Bull.* **47**:824-826, 1947.
46. Young, R. H., and Yeager, L. B. Cyanosis secondary to ink-stained athletic shirts. *Quart. Bull., Northwestern Univ. M. School* **21**: 250, 1947.
47. Dolan, R. A. Severe delayed reaction to penicillin. *Canad. M. A. J.* **57**:167, 1947.
48. Hopkins, J. G., and Lawrence, H. Sensitization to penicillin. *J. Allergy* **18**:251-262, 1947.
49. Templeton, H. J., Lunsford, C. J., and Allington, H. V. Cutaneous reactions to penicillin. *Arch. Dermat. & Syph.* **56**:325-338, 1947.
50. Kiel, V. L. Pyoderma gangrenosum in ulcerative colitis: report of case. *Arch. Dermat. & Syph.* **56**:187-190, 1947.
51. Levey, S., and Smyth, C. J. Effect of 2,3-dimercaptopropanol (BAL) on toxicity of gold. *J. Lab. & Clin. Med.* **32**:1364-1369, 1947.
52. Clayton, W., Howard, A. J., and Thomson, D. Treatment of mustard gas burns. *Brit. M. J.* **1**:797-799, 1946.
53. Aldrich, R. H. Undecylenic acid in treatment of pruritus ani and pruritus vulvae. *Indust. Med.* **16**:491, 1947.
54. Benedek, T. Pompholyx and occupational dermatitis. *Indust. Med.* **16**:344, 1947.
55. Hanzlik, P. J., Lawrence, W. S., Fellows, J. K., Luduena, F. P., and Laqueur, G. L. Epidermal application of diethylene glycol monoethyl ether (carbitol) and some other glycols. *J. Indust. Hyg. & Toxicol.* **29**:325-341, 1947.
56. Henry, S. A. Occupational cutaneous cancer attributable to certain chemicals in industry. *Brit. M. Bull.* **4**:389, 1947.
57. Schwartz, L. Occupational pigmentary changes in skin. *Arch. Dermat. & Syph.* **56**:592-600, 1947.
58. Klauder, J. V., and Brill, F. A. Correlation of boiling ranges of some petroleum solvents with irritant action on skin. *Arch. Dermat. & Syph.* **56**:197-215, 1947.
59. Tulipan, L. Acne rosacea: vitamin B complex deficiency. *Arch. Dermat. & Syph.* **56**:589-591, 1947.
60. Sachs, W., Mackee, G. M., and Rothstein, M. J. Acrodermatitis pustulosa perstans (so-called pustular psoriasis). *Arch. Dermat. & Syph.* **56**:766-770, 1947.
61. Caro, M. R., and Senear, F. E. Psoriasis of hands: nonpustular type. *Arch. Dermat. & Syph.* **56**:629-633, 1947.
62. Brunsting, L. A., and Mason, H. L. Porphyria with cutaneous manifestations. *Proc. Staff Meet., Mayo Clin.* **22**:489-494, 1947.
63. Dunsky, I., Freeman, S., and Gibson, S. Porphyria and porphyrinuria: report of case: review of porphyrin metabolism with study of congenital porphyria. *Am. J. Dis. Child.* **74**:305-320, 1947.
64. Thannhauser, S. J. Eosinophilic granuloma of bone synonymous with Schüller-Christian disease, lipid granuloma, essential xanthomatosis of normocholesteremic type and eosinophilic xanthomatous granuloma. *Arch. Int. Med.* **80**:283-285, 1947.
65. Glusman, M. Syndrome of "burning feet" (nutritional melalgia) as manifestation of nutritional deficiency. *Am. J. Med.* **3**:211-225, 1947.
66. Lloyd, C. W., and Williams, R. H. Endocrine changes associated with Laennec's cirrhosis of liver. *Am. J. Med.* **4**:315-330, 1948.
67. Editorial. Amino acid acceleration of wound healing. *J. A. M. A.* **131**:1061, 1946.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 35081

PRESENTATION OF CASE

First admission. A twenty-five-year-old single laborer entered the hospital because of varicose veins.

The patient was first seen in the Out-Patient Department three years previously for intermittent pain in both legs, occasionally associated with swelling. During the next three years he experienced occasional cramps in the legs and developed small, chronic, 1-cm. ulcers above the medial malleoli. Physical examination was otherwise negative. A bilateral, long saphenous ligation was performed. The ulcers healed readily but about two months later reappeared.

Second admission. He re-entered the hospital, where venograms indicated a blockage of the deep system. A bilateral lumbar sympathectomy was performed and dermatome grafts applied following excision of the leg ulcers. Positive blood Hinton and Wassermann tests were discovered, and he was discharged to the Out-Patient Department for treatment with mercurials and bismuth. The spinal-fluid serologic findings were negative. During the mercurial therapy he developed jaundice and albuminuria, and mercury was temporarily discontinued.

Third admission (five years later). During the interval the patient was seen periodically in the Out-Patient Department. The leg ulcers persisted without much change. The symptoms were improved, although he did not return to work. The day before this admission he had a hemoptysis (a cupful of bright-red blood). Physical examination revealed a nasal septal defect, distended pulsating neck veins, an enlarged heart, with a prolonged rough apical systolic murmur and accentuated pulmonic second sound, and generalized edema, particularly in the legs. The blood pressure was 110 systolic, 75 diastolic. A blood Hinton test was negative. The venous pressure was equivalent to 320 mm. of water. The blood and urine examinations were negative. An x-ray film showed a heart enlarged in all directions. There was prominence of the pulmonary conus. The main branches of the pulmonary artery were likewise dilated. There was no evidence of pleural fluid. The lung fields were not remarkable except for the dilated blood vessels. Fluoroscopy showed marked pulsation of the main pulmonary artery, but little pulsation of the hilar shadows. There was no enlargement of the left auricle; the aortic knob was almost absent.

An electrocardiogram showed right-axis deviation with evidence of right ventricular strain. The patient remained in the hospital about two months on a low-sodium diet, ammonium chloride and digitalis, during which he had a good diuresis. He had some paranoid and hallucinatory episodes.

Fourth admission (two and a half months later). He re-entered the hospital because of gradually increasing dyspnea and edema. In addition to the previous physical findings there was anasarca, a slightly enlarged liver and ascites. He remained in the hospital for three weeks under digitalis, mercupurin and urea treatment. The total serum protein varied between 5 and 6 gm. per 100 cc., and the nonprotein nitrogen ranged from 25 to 60 mg. per 100 cc.

Fifth admission (six months later). He was readmitted to the hospital because of an episode of hemoptysis. At this time he had massive edema. X-ray examination showed no evidence of intrapulmonary hemorrhage. Findings in the chest were much the same as those on last examination except for the transverse diameter of the heart, which was now 18 cm. compared to 17 cm. six months previously. An electrocardiogram showed auriculoventricular block, with findings consistent with chronic cor pulmonale.

Sixth admission (two years later). He was followed in the Out-Patient Department, with occasional exacerbation of the edema and treatment of the persistent leg ulcers. He re-entered the hospital with edema, more pronounced dyspnea, and complaining of yellow spots before his eyes. An electrocardiogram showed right-axis deviation and bigeminy. Digitalis was withheld temporarily, with disappearance of the bigeminy and the visual symptoms. During his hospitalization he exhibited several acute psychotic episodes with paranoid delusions. The total protein was 4.1 gm., and the nonprotein nitrogen 42 mg. per 100 cc.

Seventh admission (four months later). At this admission he exhibited marked generalized edema. The total serum protein was 3.94 gm. per 100 cc., with an albumin-globulin ratio of 1.1. The sodium was 129.9 milliequiv., the chloride 92 milliequiv., and the carbon dioxide 22.3 milliequiv. per liter; the nonprotein nitrogen was 42 mg. per 100 cc. An x-ray examination showed the heart to be slightly larger than on the previous examination, and there was definite evidence of fluid in each pleural cavity (Fig. 1). Some pulmonary edema was present, particularly in the left-upper-lung

field. He was discharged after about two weeks and remained at home for three weeks.

Final admission. He was admitted finally with generalized anasarca and gangrene of the right third and fourth toes.

He had loss of memory for recent events. There was pronounced venous distention in the neck. Both lung bases showed dullness to flatness, with diminished breath sounds and fine, moist crackles. The left cardiac border was percussed 3 cm. to the left of the midclavicular line. A Grade IV harsh systolic murmur was present, most marked near the apex. The pulmonic second sound was greater than

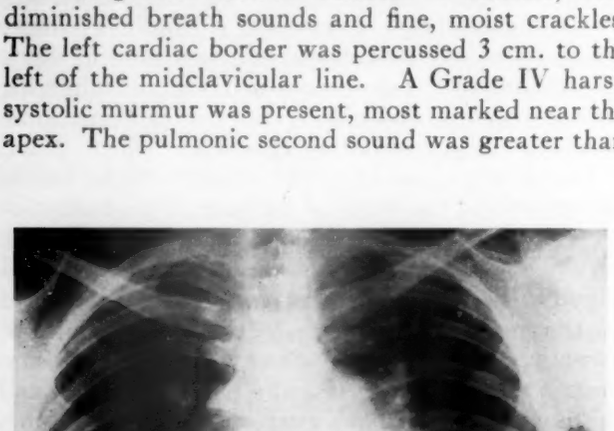

FIGURE 1.

the aortic second sound. The abdomen was tense, with pitting edema of the abdomen, flank dullness and a fluid wave.

The blood pressure was 110 systolic, 70 diastolic.

Examination of the blood showed a hemoglobin of 10 gm. and a white-cell count of 17,650, with 90 per cent neutrophils.

Following admission the patient became more disoriented and had a hemoptysis (about 150 cc. of bright-red blood). Although transferred to a psychiatric ward, his management became so difficult that transfer to a state sanatorium was necessary after about ten days.

He died about five days following the transfer.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND: When Dr. Castleman asked me to discuss this case he said that I must have seen this patient at some time. He said that did not matter, however; the implication was evident. He even offered to let me abstract the record, but I thought that that might be too confusing so I did not do that. I have studied the x-ray films, however, with the X-ray Department.

It is always annoying for the discusser to ask for something that is not available, and I am sure someone has spent many hours abstracting this long record; but before I start I really ought to know whether or not this man was cyanotic.

DR. J. H. MEANS: Yes, he was.

DR. MORTON SWARTZ: No, he was not cyanotic. That was one of the striking features.

DR. TRACY B. MALLORY: There seems to be a discrepancy, but I think it varied on different entries. There are a number of comments that he was not cyanotic, and others that he was.

DR. MEANS: I would swear that I had seen him when he was at least somewhat cyanotic.

DR. BLAND: The original red-cell count might help.

DR. MALLORY: On the first admission there was a single red-cell count of 6,500,000, followed within a week by a count of 5,100,000 and one of 4,800,000. All subsequent counts were within normal range.

DR. BLAND: In any event we must explain this patient's pulmonary hypertension. The evidence is quite clear that that existed to an extreme degree. His main pulmonary artery was large and pulsating. He had a loud pulmonic second sound, and the heart failure was limited to the right side. Mitral stenosis is the commonest cause of pulmonary hypertension. He did not have mitral stenosis for several reasons. The lungs remained uncongested throughout his illness. This much heart failure secondary to mitral stenosis without congestion of the lungs could not exist. I question the statement of slight pulmonary edema on one occasion. There was no intracardiac calcification. That is not always present, however, with mitral stenosis. He had two years of heart failure and did not fibrillate. That would be most unusual if there were an important element of mitral stenosis. Besides, the X-ray Department said that the left auricle was not large. They make mistakes on that score, but nevertheless, I am certain that his pulmonary hypertension and heart failure were not due to rheumatic heart disease and mitral stenosis.

We are left with two broad possibilities. He had either some congenital lesion of the heart, which increased the amount of blood flow through the lungs, or something in the lungs in the pulmonary vascular bed, which gave him pulmonary hypertension. This morning I was told that it was all right to look at the x-ray films with the X-ray Department, and I urgently needed their help in this connection, especially to differentiate congenital defect from obstruction in the pulmonary circuit.

As to the presence of cyanosis, different opinions have been expressed. Most people with heart failure get a little dusky at times, but I think it is safe to assume that this patient was not constantly cyanotic. In viewing the films I was left with a different impression from that obtained from

the written report, especially as regards the density of the lung roots. Dr. Wyman, would you discuss the films?

DR. STANLEY M. WYMAN: As I understand from the record, these films begin and end in the last two-year period of the patient's illness and do not include the first admission. The most striking feature of the original examination is the markedly enlarged heart, the enlargement being more impressive toward the right than toward the left. In addition to that there was a very large main pulmonary artery. The aortic-knob shadow is lost in this region. I cannot identify it with certainty on any film so that it must be at most of normal caliber if not small. The vascular shadows extending into the lung at the right hilus are definitely more prominent than usual, and on the left there is still greater enlargement of the main branches. This prominence of the vascular pattern extends into the lung field, and I think possibly it is a little more pronounced in the left lung than in the right. I believe that the patient had on first admission a very small quantity of fluid in the right pleural space. The record in the X-ray Department stated that pulsations of the cardiac borders were of good amplitude, slow and regular. They described increased prominence of the amplitude of pulsation of the main pulmonary artery, but no hilar dance. They do not say whether or not absence of pulsations of the hilar arteries was ever observed. I think the lateral view shows the heart extending far upward along the sternal border, suggesting right ventricular enlargement, and there is a high pulmonary artery here arching in this fashion and in back of the main pulmonary artery a branch that is very large. There is just the faintest suggestion of the aortic arch above the pulmonary artery. As Dr. Bland has pointed out, we did not think that the left auricle was enlarged.

The right anterior oblique view shows the trachea and the bifurcation of the main bronchi with a definite compression of the left main bronchus about 4 cm. beyond its origin. I take this process to be due to unusual enlargement of the left main branch of the pulmonary artery. I cannot outline the diameter because I cannot separate it from the other overlying shadows. The other examinations were taken subsequently — these films were a year and four months after the original films and show the heart to be slightly larger and the vascular engorgement, if anything, to be slightly more pronounced. I agree with Dr. Bland that I cannot be sure of the pulmonary edema described at one point in the left-upper-lung field. The film taken two years after the original films shows still further cardiac enlargement, and I think that the left hilar vascular shadow is increased still further and perhaps out of proportion to the increase in the right. There is a knob of density on the right just above the right main bronchus, which I believe is the azygos vein. The best I can say on this is that the heart is enlarged, probably chiefly right ventricular and right auricular, with a huge main pulmonary artery and branches, particularly the left hilar branches, which seem to have increased in size out of proportion to the right.

DR. BLAND: I would like to know the extent of pulsation in these hilar vessels beyond the main stems.

DR. WYMAN: I do not know that.

DR. BLAND: The implication is that it was present but not striking.

DR. WYMAN: It certainly was not increased.

DR. BLAND: You do not find evidence of old or recent infarcts?

DR. WYMAN: No, we looked particularly for infarcts and we were unable to see any clear-cut evidence.

DR. BLAND: This man bled a fair amount on several occasions. There was a statement in the record that there was no x-ray evidence of intrapulmonary bleeding. I cannot quite follow that.

DR. WYMAN: I do not believe that by x-ray study one can say that a lesion in the lung is hemorrhagic unless asked a specific question and there is a good history to go with it. In the past we have seen hemorrhage lying peripherally in the lung field in a large circumscribed area, not having the distribution of infarct and having a homogeneous character with borders of poor definition. When lesions of this character have cleared up promptly we have assumed them to be hemorrhage. One such case discussed at one of these conferences perhaps a year ago, but not published, actually was removed surgically and proved to be hemorrhage.

DR. BLAND: So the point is that you do not see anything that suggests a hematoma in the lung?

DR. WYMAN: No.

DR. BLAND: The first possibility that occurred to me in reading through the record was auricular septal defect. After seeing the films I am willing to discard that for several reasons. With auricular septal defect a tremendous volume of blood circulates around and around through the pulmonary system, and by cardiac catheterization it has been shown that the cardiac output with this defect is tremendous, at times up to 25 or 30 liters of blood, with only 3 or 4 liters going to the periphery. That indicates a great amount of blood circulating through the lungs. Under these circumstances the lung roots are massive. Therefore, I think we can safely discard that possibility after viewing the films.

What other congenital lesions should we consider that are noncyanotic at birth and yet may become slightly cyanotic later? One is the so-called Eisenmenger's complex, which is a modification of the tetralogy of Fallot. In this condition cyanosis usually appears in adolescence, and later with heart failure the patients are apt to be extremely blue. This does not quite fit the picture here. I cannot

think of any other congenital derangement that we need consider seriously. Another remote possibility is arteriovenous fistula in the lung, which we now and then see producing strain on the right side of the heart. It is usually evident by x-ray study and is apt to produce bruits.

I am forced back for a diagnosis to the pulmonary vascular bed itself — either primary or secondary obliterative disease of the pulmonary arterial tree. One possibility is pulmonary obstruction secondary to chronic lung disease. This man gave no history of chronic pulmonary disease. He never coughed, wheezed or raised significant sputum, and there was no evidence to suggest it by x-ray study. Of course, extensive lung fibrosis with cor pulmonale can exist without much x-ray evidence in the lung itself. Is that true, Dr. Wyman?

DR. WYMAN: Absolutely true.

DR. BLAND: Can it exist to that degree, Dr. King, without symptoms pointing to pulmonary disease in the way of cough, wheeze or sputum?

DR. DONALD S. KING: Almost never.

DR. BLAND: This patient had no lung disease. Therefore, we are left with the pulmonary arterial bed as the likely cause of his trouble. We have studied here, and Dr. Castleman is now in the process of reviewing pathologically, about 12 patients with so-called primary disease of the vascular bed itself involving a variety of processes but most often an obliterative endarteritis of the smaller vessels and of unknown etiology. We have seen it in an infant a few months of age. In most cases in which we have puzzled over the cause of cor pulmonale and have not been able to identify a congenital lesion of the heart or chronic disease of the lungs, our experience has been that it usually turns out to be pulmonary endarteritis, unexplained. I am betting heavily on that possibility here. In some of the cases we are reviewing, the changes in the pulmonary vessels are secondary to showers of small emboli. Dr. Castleman and I[1] reported a case two years ago of a patient we had observed clinically for eight years with a large heart and right-sided failure. The vascular system in the lungs was different from any of the others. The obstruction was limited throughout both lungs to the tertiary vessels, and some had recanalized. Elsewhere in the vascular tree there was no obstruction. The lungs were all right. We could not explain this widespread uniformly localized obstruction except that at some time or other there had been showers of emboli, all of about the same size, that had plugged these tertiary vessels throughout the lungs. There has been an occasional patient who, secondary to disease elsewhere in the body, has developed secondary thrombi in situ in the main pulmonary stems. Drs. Means and Mallory[2] long ago reported such a case in which there was thrombosis and obstruction of the main pulmonary trunk. A few months ago a case was discussed here in which the X-ray Department had cleverly pointed out two large pulmonary stems, one of which pulsated vigorously and was accompanied by increased vascular roots all the way out in the lung, whereas the other pulsated for a short distance and the lung was relatively avascular beyond that point. It was suggested that there must be a local pulmonary thrombus in that main vessel, and this proved to be true at autopsy. Our patient today had serious peripheral vascular disease, both arterial and venous, and had had episodes of bleeding in the lungs. The interpretation of these episodes has bothered me somewhat since with primary arterial disease in the lungs there is usually no bleeding. Actually, the blood does not adequately get to the lungs. It is pulmonary ischemia. They may or may not be cyanotic.

In conclusion I think this patient had obliterative vascular disease of the lungs. Furthermore, I believe it must have been primarily of the small vessels rather than of the large pulmonary trunks.

DR. MEANS: I saw this man on several admissions, and my recollection of this case is fairly vivid. But I am a little let down because I cannot find on studying the record a statement that he was cyanotic, although I have a vivid recollection that on the last admission he was somewhat cyanotic. To make a long story short, everyone knew that he had some sort of cor pulmonale, but what kind was the question. A note made by Dr. Wheeler in 1945 is worth reading: "The Cardiac Group believes that this patient has chronic cor pulmonale, probably on the basis of pulmonary arterial obliterative disease. Constrictive pericarditis seems to be well ruled out by the x-ray and electrocardiographic findings, so that exploration of the heart does not seem advisable." We did not get any further than that. On several subsequent admissions he had cor pulmonale and chronic insufficiency, and no one knew beyond that just what the situation was. I wrote last November in the record: "As far as I can make out the fundamental nature of this cardiopathy remains a mystery. Cor pulmonale, yes, but due to what? I would still cling to the possibility of pulmonary-artery thrombosis. He has tight ascites, which diuretics no longer relieve completely. I see no objection to an abdominal tap as symptomatic treatment." That is all I contributed to this situation. We might later come back to the case Dr. Bland mentioned.

DR. BLAND: I assume that this patient's heart was not catheterized? That would have excluded a shunt.

DR. MALLORY: It was considered and believed to be too dangerous.

DR. HAROLD E. ELRICH: He had Buerger's disease of the leg. Do you think there is any tie-up between pulmonary-artery disease and that?

DR. BLAND: That always comes up, and it is hard to answer. I do not know of any relation between the two. Do you, Dr. Mallory?

DR. MALLORY: Buerger's disease has been claimed to involve the lungs. I do not know the evidence, however, and I have never seen it myself.

DR. BLAND: I think we can discard syphilis without serious thought.

DR. WYMAN: I wonder if Dr. Bland attaches any significance to the apparent discrepancy in size of the two main hilar branches of the pulmonary artery.

DR. BLAND: That was fairly striking and is suggestive of unilateral thrombosis.

DR. WYMAN: The larger left hilar shadow is associated with apparently larger vessels throughout the left lung. It is very disturbing to make a diagnosis of thrombosis in the main pulmonary artery.

DR. BLAND: Unless it happened at this point (on the film).

DR. WYMAN: Yes, in back, and you cannot see it.

DR. BLAND: Is it fair to give Dr. King a chance since this involves the lungs?

DR. KING: I had a similar case a year ago with phlebitis and varicose ulcers and cor pulmonale, and my guess was emboli, multiple small pulmonary emboli. I was wrong; it was primary vascular disease, so my inclinations here would be to make this primary chronic pulmonary vascular disease, as you have done.

DR. MEANS: Can I ask Dr. King what kind of chronic pulmonary vascular disease?

DR. KING: I think it was called arteriosclerosis, if I remember correctly.

DR. BLAND: Dr. Wyman wants to put a thrombus in the main right-pulmonary-artery stem behind the heart where it cannot be seen.

CLINICAL DIAGNOSIS

Cor pulmonale, cause undetermined.

DR. BLAND'S DIAGNOSES

Obliterative pulmonary-artery disease.
Cor pulmonale.
Congestive failure.
Peripheral vascular disease (venous and arterial).

ANATOMICAL DIAGNOSES

Embolism and thrombosis of pulmonary-artery tree, diffuse, with organization and recanalization.
Cor pulmonale.
Thromboangiitis obliterans, leg vessels?
Ascites.
Operative wound, old, lumbar sympathectomy, bilateral.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Autopsy showed a large thrombus in the main pulmonary artery, beginning 3 cm. distal to the valve. It then extended to the bifurcation and spread into both hilar arteries, completely occluding the one on the left and only partially occluding the one on the right. The cut surfaces of the lung parenchyma showed that all the vessels throughout both lungs were prominent and stiff and stood out from the surface. In many of them it was quite evident that the lumen had been at one time obliterated since small canalizing vessels were present within the larger ones. This process extended down to the most minute vessels in the lung.

In the upper right-hand corner of the microscopical slide can be seen a vessel that has been divided in two by a band of fibrous tissue, with two canalizing vessels on each side. In this next field is a vessel that has been divided into half a dozen different lumens by multiple fibrous septums. Here is a vessel with very marked intimal thickening and a single lumen, very much hypertrophied. Here are several extensively recanalized small vessels.

One is still left with the question of etiology of this process. It involves pulmonary arteries of all sizes from the main pulmonary artery down to the smallest arterioles — fairly uniformly distributed throughout both lungs. The changes all seem to be internal to the internal elastic lamina; there are no changes in the media of the vessels. They can all be explained on the basis of multiple pulmonary emboli with organization and recanalization, followed by a retrograde thrombosis going back into the main arteries. I do not see any way that I can prove that is the case. It is not very different from what has been described as primary endarteritis except that the multiplicity of the canalizing vessels is much more like organization of emboli.

DR. GORDON S. MYERS: Was any source for emboli found?

DR. MALLORY: There was extensive disease of both arteries and veins in the legs, with almost complete obliteration of the left femoral artery about 6 cm. below Poupart's ligament. None of the changes at the time of autopsy were characteristic of Buerger's disease; and the original biopsy, to my eye, was not characteristic either. The biopsy showed a large vein, which looked like a recanalized varicose vein and not particularly like Buerger's disease. But Buerger's disease is only specific in its histology for a brief period in the acute stages. In later, chronic stages one can only guess about it.

DR. MYERS: Did this disease involve the capillaries as well as the arterioles?

DR. MALLORY: It went as far as the smallest arterioles, but no capillaries were involved that I could make out.

DR. MEANS: If there was an embolus large enough to shut off one main branch of the pulmonary artery, would it not have been suddenly fatal?

DR. MALLORY: I suppose so.

DR. MEANS: If due to embolism, we must assume small ones and subsequent retrograde thrombosis.

DR. MALLORY: That is possible. We found no evidence of infarct, however, which would help back up such an opinion.

DR. MEANS: Am I right in thinking that in the case we reported no such extensive process in the small arterioles prevailed? The process was largely confined to the right main pulmonary artery, which was totally occluded just as this one was. A point of interest in that case was that the bronchial artery was huge, about as large as my finger, and furnished nutrition to the lung adequately. In this patient the autopsy was done elsewhere, and the tissue was in such a state that you could not determine whether or not the bronchial artery was enlarged.

DR. MALLORY: In the microscopical sections we could identify apparently enlarged branches of the bronchial artery but were unable to identify the main trunk.

REFERENCES

1. Castleman, B., and Bland, E. F. Organized emboli of tertiary pulmonary arteries: unusual case of cor pulmonale. *Arch. Path.* **42**: 581-589, 1946.
2. Means, J. H., and Mallory, T. B. Total occlusion of right branch of pulmonary artery by organized thrombus. *Ann. Int. Med.* **5**: 417-427, 1931.

CASE 35082

PRESENTATION OF CASE

A seventy-three-year-old widow entered the hospital complaining of epigastric pain with vomiting.

Four weeks prior to admission she suffered an episode of dull, nonradiating, epigastric pain with nausea, vomiting, diarrhea and a temperature of 101°F. She was seen by her physician, and a diagnosis of acute gastroenteritis was made. About one week later she began to experience almost daily episodes of steady, epigastric pain, lasting for two or three hours and relieved by morphine. These attacks were associated with nausea and occasional vomiting. There was probable aggravation of the pain by the taking of food. No history of right-upper-quadrant pain, fatty-food intolerance or jaundice was elicited. There were no previous symptoms suggestive of ulcer. She had lost about 15 pounds during the month prior to admission.

Twenty years previously a pelvic operation was performed, the exact nature of which was not known.

Physical examination revealed a senile, uncooperative, slightly disoriented, elderly woman. The heart was not enlarged, the aortic second sound was greater than the pulmonic second, and a Grade I systolic murmur was present at the apex. There was diffuse abdominal tenderness, most marked in the right lower quadrant and midepigastrium, with slight muscular spasm in the epigastrium. No masses were felt, and no peristalsis was heard. She was retching during part of the examination. A lower abdominal, midline scar was present.

The temperature was 98.6°F., the pulse 120, and the respirations 22. The blood pressure was 175 systolic, 80 diastolic.

Examination of the blood showed a hemoglobin of 14 gm. and a white-cell count of 15,950, with 89 per cent neutrophils. Urinalysis was negative. A serum amylase was 45 units per 100 cc., the chloride was 104 milliequiv. per liter, and the nonprotein nitrogen was 18 mg. per 100 cc. A chest x-ray examination appeared normal. There was no free air under the diaphragm. A plain film of the abdomen showed a moderate amount of gas scattered throughout the large bowel. One small loop of gas-filled small bowel was present in the left upper quadrant. This did not have the appearance of a small-bowel obstruction. There was one small oval calcification, 3 mm. in diameter, present in the right side of the abdomen adjacent to the right border of the second lumbar vertebra. This appeared to be outside the kidney. Its exact nature could not be determined.

Following admission she complained of increased abdominal pain. The white-cell count twelve hours after admission was 22,000; the blood pressure was 125 systolic, 70 diastolic, and the pulse 160. She was observed for several hours and was noted to have intermittent episodes of severe abdominal pain, which was apparently generalized and caused her to writhe in bed and to double herself up. During these episodes some hyperactive peristaltic sounds were heard. During this period the crampy pain was unrelieved by calcium gluconate intravenously. During the period of observation she developed obvious signs of shock characterized by a falling blood pressure and a rising pulse. About sixteen hours following admission an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT R. LINTON: This elderly woman obviously entered the hospital with some sort of acute abdominal condition, which, I believe, was surgical. The history is of interest in that the symptoms began one month before she was admitted to the hospital. They were characteristic of something affecting the gastrointestinal tract, since she had nausea and vomiting and associated with that she also had severe pain, apparently sufficient to require morphine — I presume by injection.

The past history is of interest in that there are symptoms suggestive of a lesion such as a duodenal or a gastric ulcer. Her dietary habits certainly make one think that she was not suffering from colitis or enteritis. I believe biliary-tract disease can be ruled out for the same reason. Perhaps of significance, especially to a surgeon, this patient with an acute abdominal condition (relatively acute at least) had had a pelvic operation twenty years before so that one cannot help considering in the differential diagnosis the possibility of intestinal

obstruction due to adhesions of the small intestine. I think it is unlikely in this particular patient, but it is something one should always think of when one sees a scar on the abdomen with an acute abdominal condition.

The physical examination was essentially negative, I think, except for the fact that she had diffuse abdominal tenderness, most marked in the right lower quadrant and epigastrium. It is of significance that the temperature was normal — 98.6°F. I presume that is to be relied upon and, if so, rules out the question of peritonitis at the time that she was admitted so that I doubt that she had a condition at that time that was producing peritonitis. The cardiovascular system was in a satisfactory condition for her age. The blood pressure was 175 systolic, 80 diastolic. She had not lost much blood, since the hemoglobin was 14 gm., unless she was dehydrated, which can elevate the hemoglobin. We have no other figure on the hemoglobin so if she was bleeding, I will have to leave that to Dr. Mallory to tell us about.

The serum amylase was 45 units per 100 cc. I believe in our laboratory the normal is somewhere in the vicinity of 30 units; is that right, Dr. Mallory?

Dr. Tracy B. Mallory: Yes.

Dr. Linton: The serum amylase was slightly elevated. Undoubtedly those taking care of her were thinking of acute pancreatitis, which one should consider in a patient complaining of epigastric pain and the other associated symptoms. I would say that 45 units of serum amylase was equivocal; it does not help one way or the other in making a diagnosis of pancreatitis. If she had pancreatitis beginning four weeks before admission, one would expect a normal serum amylase after that long a period. As a matter of fact, the determination usually returns to normal fairly promptly when an acute pancreatitis develops — I think within a matter of forty-eight hours. The other point regarding serum amylase is that it is a test that cannot be relied on too much to make a diagnosis of pancreatitis because there are other acute abdominal conditions, even biliary-tract disease, that give an elevation, as I believe this patient demonstrates, although the elevation was not very marked.

The nonprotein nitrogen was normal. From the surgical point of view the x-ray films are of interest in any patient who has an acute abdominal condition in which one suspects intestinal obstruction, and I think one would suspect it in this case.

Dr. Stanley M. Wyman: The posteroanterior film of the chest shows the lung fields grossly clear. The heart shadow is not remarkable for a woman of this age. There is no evidence of gas beneath either leaf of the diaphragm. The liver shadow and the spleen do not appear unusual. The lateral view of the chest shows an increase in the anteroposterior diameter, I believe, in keeping with the patient's given age. Plain films of the abdomen show again that the liver is grossly normal, and the spleen not enlarged. This one loop of gas-filled bowel certainly suggests small bowel, probably jejunum, and it is wider than usual; but I think it is insufficient evidence to make a flat-footed diagnosis of intestinal obstruction. I believe the small, round shadow of calcification described may possibly lie in cartilage. The bones are osteoporotic but show no definite destruction. I cannot identify any unusual soft-tissue masses.

Dr. Linton: A plain abdominal film in a patient whom one suspects of having intestinal obstruction is an extremely important diagnostic aid because by means of it one can frequently detect early intestinal obstruction and certainly can readily detect an advanced intestinal obstruction. My opinion on looking at these x-ray films and listening to Dr. Wyman's description of them is that this patient obviously did not have intestinal obstruction of sufficient degree to explain the nausea and vomiting — as well as the fact that she had diarrhea, which would be hard to connect with intestinal obstruction. The x-ray film on the left shows even less gas than one usually sees in a plain abdominal film. Do you agree?

Dr. Wyman: That is true. On the far right there is a little gas in the colon and in the one loop that represents presumable jejunum.

Dr. Linton: I feel quite sure then that we can rule out intestinal obstruction as the cause of her symptoms. The white-cell count twelve hours after admission was 22,000, indicating some pathologic process sufficient to increase the count which, as a matter of fact, increased from 16,000 to 22,000. Of extreme significance, I think, is the fact that the blood pressure dropped to 125 systolic, 70 diastolic, and that the pulse rose to 160. Something was going on within the abdomen that had produced these changes, which apparently had been rather dramatic as they came on within twelve hours of admission. Associated with that she had the terrific bouts of pain that made her writhe about. Her condition did not improve. The peristaltic sounds in the abdomen were not particularly marked; some were hyperactive, which I cannot make much out of. Someone must have thought she had either common-duct colic or ureteral colic because calcium gluconate was given, intravenously, I presume. But as one might expect, it did her no good. She obviously was getting worse, and for that reason she was taken to the operating room for an exploratory laparotomy.

In summary, I think that she had something involving the intestinal tract. I do not believe it involved the stomach. It was not acute appendicitis with peritonitis, for I believe the condition had been going on too long. One always thinks of appendicitis, even in this elderly age group. It seems unlikely that it was a malignant lesion. At least we have insufficient evidence to make a diagnosis of

cancer of the large or small bowel. I think the most likely diagnosis in this case is thrombosis of the mesenteric vessels, either veins or arteries. And in view of the fact that this condition had been going on for several weeks, I would say that it was venous thrombosis of the mesenteric vessels, probably the superior mesenteric vein.

DR. CHESTER M. JONES: Is the first film at all suggestive of free fluid in the abdominal cavity? There is a ground-glass appearance over the entire abdominal area.

DR. WYMAN: One cannot judge, because the film was taken for the chest primarily. Therefore, there was insufficient penetration of the abdomen, and one would find this appearance even in normal persons.

DR. JONES: If that were an ordinary abdominal film, it would be exciting.

DR. WYMAN: Absolutely.

DR. F. DENNETTE ADAMS: Can you, so to speak, rule out obstruction when there is no dilated bowel? In other words, if this condition is present, does it work just as well in reverse?

DR. WYMAN: I think one may miss dilated loops readily on a film taken in the supine or prone position. We have been fooled in such cases because the bowel was filled with fluid, obscuring the gas shadows to a great extent. If these people are placed upright, the fluid levels are readily apparent.

DR. LINTON: The gas in the right-hand film is in the colon. Therefore, she could not have had small-bowel obstruction, and she was too sick to have had large-bowel obstruction, I believe.

CLINICAL DIAGNOSIS

Perforated carcinoma of stomach.

DR. LINTON'S DIAGNOSIS

Acute mesenteric thrombosis, venous.

ANATOMICAL DIAGNOSES

Infarction of small intestine, cause undetermined.
Arteriosclerosis, generalized, severe aortic, slight coronary and mesenteric.
Nephrosclerosis, moderate.
Polyp of cecum.

PATHOLOGICAL DISCUSSION

DR. MALLORY: I do not see either Dr. Scannell or Dr. Moorman in the audience. They operated on this patient and found on entering the abdomen diffuse discoloration of the small bowel, beginning about 16 cm. below the ligament of Treitz and extending almost down to the ileum. They could not feel pulsations in the vessels of the mesentery. Going back to the aorta they were able to feel pulsations of the trunk of the superior mesenteric artery for a distance of 1.5 or 2 cm., where there was a zone that felt a little thickened where the pulsations disappeared. They made a diagnosis of thrombosis of the superior mesenteric artery and believed that any surgical treatment was impossible in view of the fact that the entire small bowel appeared to be involved. The patient died about twelve hours later.

At the time of autopsy the resident pathologist, having had experience with a very similar case, refused to dissect the mesenteric vessels until both surgeons taking part in the operation were present. The three of them then examined the vessels with extreme care, and no thrombus was found anywhere in the distribution of the mesenteric artery. On the other hand, the entire small bowel was completely gangrenous by that time. The veins of the mesentery were likewise entirely free from thrombi so that there appears to have been a functional occlusion of the mesenteric artery with no anatomic basis and a strong suggestion that it was spastic in origin. The question of spasm in an intra-abdominal vessel is one that has been debated a great deal. Many people are skeptical of it. Dunphy,* at the Peter Bent Brigham Hospital, was interested in it a few years ago and concluded that in many cases functional obstruction of the mesenteric artery alone could produce episodes of acute intra-abdominal pain, often preceding a final thrombosis. He argued that this might be spastic occlusion of the artery analogous to anginal attacks in the coronary arteries.

DR. JONES: Were the arteries sclerosed?

DR. MALLORY: They were markedly sclerosed.

DR. LINTON: I still cannot believe that at the age of seventy-three a vessel can go into spasm, especially spasm sufficient to shut off a vessel.

DR. MALLORY: The last time we reported such a situation the surgeons refused to believe it. That is why the resident insisted on their presence. They actually dissected the vessel under our eyes. We convinced them at any rate. Whether I can convince this audience, I do not know.

DR. LINTON: It is a most extraordinary and interesting lesion. I have never heard of it.

DR. JONES: Dr. Linton commented that at this age there could not be spasm of the vessels. In coronary disease older people with stiff arteries get angina, not necessarily because of spasm but because of the extra demands on the artery at certain times, producing coronary insufficiency. After meals there may be a great demand on the mesenteric circulation that might be analogous.

DR. LINTON: You mentioned that the superior mesenteric artery was occluded at the time of operation. It would be hard to imagine a vessel as large as my little finger being shut off by spasm, but I must admit one cannot refute the findings Dr. Mallory has reported. I still say that this is a most unusual and interesting case of vascular disease.

*Dunphy, J. E. Abdominal pain of vascular origin. *Am. J. M. Sc.* **192**: 109-113, 1936.

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ENDS AND MEANS

The correspondence printed elsewhere in this issue of the *Journal* mainly concerns the action of the American Medical Association in assessing each member twenty-five dollars; only secondarily or by implication do the writers of the letters refer to compulsory health insurance or any other phase of Government participation in medicine. By an ironic turn of circumstances, these men, who have no quarrel with the Association's stand on state medicine, strongly object to the so-called "enforced" contribution, part of which was earmarked by their spokesmen as an aid in the struggle against changes imposed by force from outside the profession. It is sobering to realize that the condemnation expressed represents division among those who are otherwise united in their opposition to dictation.

Among the liberties that doctors at present possess is freedom to criticize — whether the object is the Government or their own spokesmen. The opinion is properly expressed through an official organ of a society of physicians, not in the correspondence columns of the lay press: the public, which in the final analysis will decide the grave question now facing the medical profession, should not be given an unwarranted impression of undue friction and bickering within the ranks.

The strength that is inherent in union should not be lost sight of in differences of opinion about the best means of serving the interests of the American public. Regarding the acceptability of the assessment, returns so far received in Massachusetts indicate an overwhelming vote of confidence, particularly on the part of the active practitioners. Additional effective ways of countering the arguments in favor of state medicine must be found. Perhaps the best method is individual action to achieve a common end, each physician being "chairman of his Public Relations Committee."[1] The physicians may justifiably point out to their patients the full implications involved; Americans, for whom such words as "social" and "socialized" have become so disarmingly familiar as to have few terrors, might well be impressed by the connotations of the word "compulsory" — the dangerous term that, as the correspondence referred to indicates, can cause discord even among those who are united on fundamental issues. If doctors, acting independently but inspired by unity of conviction and determination, could demonstrate to their patients the achievements of free medicine in America (and the consequent benefits to the people at large) and the best means of maintaining and extending these benefits, public pressure could cause legislators to consult the medical profession in the drafting of plans and regulations vitally affecting medical practice.

Thus might the American doctor and his patient be spared the evils of Government-directed medicine as reported by one who has witnessed them at first hand: "Had they [the British medical profession] analyzed the defects in their system, presented a well conceived plan for improvements, and then

stood fast against ill advised changes, the British people might now be receiving better care and the physicians might be happier about their working milieu. . . ."[2]

REFERENCES

1. Editorial. Medical public relations. *J. Indiana State M. A.* **42**:29, 1949.
2. Sweet, W. H. Recent impressions of medical practice in Great Britain. *New Eng. J. Med.* **240**:168-173, 1949.

ANOTHER BULWARK AGAINST SOCIALIZED MEDICINE

SOUND public-health programs providing statewide coverage can best be administered through the establishment of efficient and economic local health departments, employing full-time, trained and experienced personnel. The American Medical Association has for many years recognized the urgent need for this type of health coverage and strongly supports sound action to extend and strengthen local health services. This support has been expressed in numerous resolutions passed by the House of Delegates and is Point 2 of the Association's Ten Point Health Program.

Through the remarkable combination of complacency, inadequate legislation and local autonomy, Massachusetts has succeeded in ignoring its local health programs, which for the most part compare unfavorably with those established in other states. An article in a recent issue of the *Journal** outlined the severe deficiencies in this field that exist throughout the Commonwealth. Where does the fault lie?

Appreciation of the need for the promotion and support of adequate local health services in Massachusetts is with few exceptions limited to practicing physicians who have knowledge and interest in their local community's health programs. Unfortunately, their numbers are few.

The solution of this critical problem lies in community interests and action. It devolves upon the physician as a member of his community to exert efforts to help obtain adequate local health services. It befits him as a member of a society actively opposed to a threatened program of socialized medicine to support accepted and necessary measures that will ensure the free practice of medicine.

*Archibald, R., Fiore, A. and Skvirsky, S. L. Local health services in Massachusetts. *New Eng. J. Med.* **239**:858-861, 1948.

The people purchase health service. Whether that purchase is accomplished directly between patient and physician or indirectly, through the tax dollar, it remains that health, as a commodity, constitutes big business, and the consumer's voice has grown louder in its demand for more service.

The physician has his choice. He may retain his complacency, ignore the demand and express open resentment of the threatened program of socialized medicine, or he may make constructive efforts to satisfy these demands by the promotion, at the local level, of adequate, basic health services through measures endorsed by the American Medical Association.

Such a program of full-time local health departments providing efficiently and economically administered health services is the physician's disturbingly obvious but as yet unrecognized weapon against the threatened advances on his right to practice independent of governmental control.

The following statement is quoted in full, as it appeared in the recent January 19 issue of the *Bulletin of the Middlesex East District Medical Society*:

> Excerpts from Mr. Ewing's speech before the State and Territorial health officers in Washington: "Success of the government health plan depends on the people themselves and what they are willing to do about it." He then stated in brief that each community must be organized, and state and local campaigns of education must be planned, and that he is putting this up to the health officers to undertake this job in their states. There it is gentlemen, and what are we, as a Medical Society, going to do about it?

It should be pointed out that *any* health program "depends on the people themselves and what they are willing to do about it" and that physicians constitute a not unimportant segment of these people. Let them look to the stark inadequacies that exist in their own local health services for their answer to the question: "What are we as a Medical Society going to do about it?"

While the Federal Security Administrator has thrown the challenge to state health officers to put across his program, there is no evidence that the health officers have accepted the challenge. As a matter of fact, health officers are the practitioner's strongest ally in his struggle against political inter-

ference. The failure on the part of many physicians to comprehend the basic underlying principles of public-health services has contributed enormously to the growth of the ever-lengthening shadow of governmental control of medicine.

Unwarranted criticism based on superficial knowledge assumes an importance second only to that of complacency in its power to destroy any unified group attack against the threat of political control.

Promotion of basic health services at the local level is sorely needed. With few exceptions, Massachusetts lags far behind other states in their efforts to satisfy these needs.

There are now before the Massachusetts General Court two bills that, if passed, will facilitate the promotion and maintenance of local health units throughout the Commonwealth. At the federal level, the eighty-first Congress has under consideration proposed legislation to further this program. Senator Virgil Chapman, who together with Senator Leverett Saltonstall and others has introduced the Local Public Health Units Act of 1949 (S. 522), has commented that the "creation of such a system would . . . constitute the surest bulwark against socialized medicine which many of us think is undesirable in America."

The physicians of Massachusetts have it within their power to strengthen that bulwark, through their support and interest in the program to provide all the people of the Commonwealth with basic local health facilities.

NATION-WIDE AND WORLD-WIDE PROGRAM FOR CONTROL OF INFLUENZA

One of the most important limitations of the protective value of vaccination against influenza is the occurrence of variations among strains of influenza virus. This fact became particularly prominent during the epidemic that occurred in the winter and spring of 1947. That epidemic was caused by a strain of influenza A that was antigenically distinct from the influenza A strains that had been incorporated in the polyvalent influenza vaccines in use prior to that time. The evidence came from the demonstration that experimental animals immunized with the standard strains that were contained in commercial vaccines failed to protect against infection with the strain that was the cause of the 1947 influenza epidemic. What is more, the incidence of influenza among persons who had been vaccinated with the commercial vaccines shortly before this epidemic was the same as that among persons who had not been vaccinated. By contrast, during the epidemic of 1945–1946, which was due to influenza B, the protection conferred by the Lee strain that was incorporated in the standard vaccines seems to have been of high grade, as evidenced by the low incidence of influenza among vaccinated persons as compared with the unvaccinated controls during that epidemic.

Another limitation in the use of influenza vaccines is the relatively short duration of the protection that results from vaccination with influenza viruses. This necessitates the administration of the vaccines within a few weeks of an anticipated influenza epidemic, and since the exact time of occurrence of such epidemics cannot be predicted with certainty, it becomes necessary to repeat vaccinations in the fall of each year before the season for respiratory infections begins. One of the outstanding features of an influenza epidemic, when it occurs in any given area, is its explosive character. Adequate protection following vaccination, however, does not usually occur in less than one or two weeks. One cannot, therefore, expect to isolate an epidemic strain from any given area, prepare a vaccine from that strain that will pass potency and sterility tests and have the vaccine distributed and administered to the exposed population in the same area in time to do any good.

Fortunately, some pandemics in the past have been preceded by small and relatively localized outbreaks before the major epidemics reached their peak in the great centers of population. If these small outbreaks can be recognized early, the strains isolated and identified and their antigenic relation to known strains that are in use in the available vaccines determined promptly, it may be possible to choose from those available or to prepare more satisfactory vaccines for use in the major epidemic. This, in turn, may considerably increase the chance

for the vaccine to have a protective effect when the epidemic strikes.

In this country the surgeons general of the Army, Navy, Air Forces and Public Health Service have developed a plan based upon this principle by which it is hoped to prevent a recurrence of a serious epidemic like that of 1918. This plan is part of an international program that was set up by the World Health Organization last year to study influenza and to aid physicians and health officers in the control of the disease. An influenza information center to serve as headquarters in the United States has been established at the National Institutes of Health in Bethesda, Maryland. The specific objectives of the world-wide program are to identify new strains of influenza virus as they appear, and to evaluate their usefulness for incorporation into influenza vaccines.

It is anticipated that as soon as a significant outbreak of a respiratory disease suspected of being influenza is reported in a given community, the Influenza Information Center will alert diagnostic laboratories in the region asking them to carry out serologic tests on patients for the presence of antibody against the influenza virus. Certain laboratories will also be asked to assign to the affected community a team of investigators experienced in the technics of isolating the virus. As soon as these investigators have isolated a new strain of virus they will send it at once for complete antigenic analysis to an established strain-study center of the Influenza Information Center, and appropriate strains of virus that have been isolated will be considered for possible inclusion in commercial vaccines.

The international influenza program was proposed during the Fourth International Congress for Microbiology in Copenhagen in July, 1947. Two months after that meeting, an international influenza center was established at the National Institute for Medical Research in London. The World Health Organization at its first World Health Assembly approved continuance of that center and recommended that all nations be invited to set up organizations to collaborate with it. In this country the appropriate authorities decided to establish the Influenza Information Center at Bethesda, Maryland, which would administer the program in this country and would serve as a liaison office between the International Influenza Center and participating American laboratories.

Obviously the key to the success of this program is the co-operation of physicians in the early recognition and reporting of cases suspected of being influenza.

RED CROSS CAMPAIGN

THE annual campaign of the American Red Cross, which will be conducted in March, once again draws attention to the needs, as well as the achievements, of that organization. Community co-operation is essential in all work done by the Red Cross, whether it is educational or preventive (instruction in first aid, water safety, accident prevention, home nursing and nutrition) or remedial (aid to veterans, servicemen and civilians, both hospitalized and able bodied). An illustration of the value of public partnership is provided by the fact that 64,000 persons have offered to donate blood, and that blood has been distributed to more than 350 hospitals. The Red Cross asks that the generous response in previous years be continued — that the people contribute the money, time and moral support necessary to make the 1949 campaign a success and to guarantee continued services in the future.

No one needs to be reminded of the achievements of the Red Cross: where the need is greatest, the help is forthcoming. Last year more than three hundred disasters occurred in widely separated communities, and organized and efficient efforts were available in the work of the community volunteers and full-time staff of the Red Cross. Everyone is urged to contribute generously to this year's campaign: community need is met by community partnership, and when disaster strikes again, the help of the Red Cross will be vital.

MASSACHUSETTS MEDICAL SOCIETY

HOTEL ACCOMMODATIONS FOR THE ANNUAL MEETING

Headquarters for the one hundred and sixty-eighth annual meeting of the Society, to be held on May 24, 25 and 26, will be at the Hotel Sheraton, 50 Franklin Street, Worcester, Massachusetts. As accommodations in the hotel are limited, it is suggested that fellows wishing to attend the meeting reserve their rooms as soon as possible.

COMMITTEE ON ARRANGEMENTS

DEATHS

CARD — Walton G. Card, M.D., of Haverhill, died on November 11. He was in his sixtieth year.

Dr. Card received his degree from Tufts College Medical School in 1925. He was a member of the staff of Hale Hospital and a fellow of the American Medical Association.

His mother, two brothers and one sister survive.

GILLON — Charles J. C. Gillon, M.D., of Taunton, died on January 15. He was in his sixtieth year.

Dr. Gillon received his degree from Harvard Medical School in 1915. He was chief of the Eye, Ear, Nose and Throat Service of Morton Hospital and consultant at Taunton State Hospital.

His widow, a son and a daughter survive.

MACKAY — William M. MacKay, M.D., of Waltham, died on January 31. He was in his sixtieth year.

Dr. MacKay received his degree from Queen's University Faculty of Medicine, Kingston, Ontario, in 1914. He was senior physician of Middlesex County Sanatorium and a fellow of the American Medical Association.

His widow, three brothers and two sisters survive.

WELLER — John H. Weller, M.D., of Bridgewater, died on November 19. He was in his seventieth year.

Dr. Weller received his degree from College of Physicians and Surgeons of Baltimore in 1909. He was senior physician at the Bridgewater State Farm and was a member of the New England Society of Psychiatry and a fellow of the American Medical Association.

His widow and a daughter survive.

POSTGRADUATE LECTURE COURSE

The fourth Postgraduate Lecture Course, which has been arranged by the Committee on Postgraduate Medical Education, Massachusetts Medical Society, in co-operation with the Massachusetts Department of Public Health, will begin on March 7. The meetings will be held at Sanders Theater in Memorial Hall, Harvard University, Cambridge. These lectures are designed for all physicians of Massachusetts and surrounding states, medical officers, hospital residents, interns, medical students and postgraduate students.

All those who plan to attend but have not enrolled should do so immediately by either returning the post card recently forwarded to all physicians in Massachusetts or addressing a post card or letter directly to Postgraduate Lecture Course Committee, Massachusetts Medical Society, 8 Fenway, Boston 15.

The detailed program for the course is as follows:

Monday, March 7. PUBLIC HEALTH. Chairmen: James S. Simmons and John F. Conlin.

7:00–7:30. **Local Health Departments.** Hugh R. Leavell, professor of public-health practice, Harvard School of Public Health.

7:30–8:00. **Maternal and Child Health.** Samuel B. Kirkwood, assistant professor of maternal health and instructor in obstetrics and gynecology, Harvard School of Public Health.

8:00–8:30. **School Health.** Stuart S. Stevenson, assistant professor of child health, Harvard School of Public Health.

8:30–9:00. **Industrial Health.** Albert O. Seeler, assistant professor of industrial medicine, Harvard School of Public Health.

Wednesday, March 9. CARDIOVASCULAR DISEASE. Chairmen: Laurence B. Ellis and Eugene Eppinger.

4:00–4:30. **The National Heart Institute.** Paul D. White, chief consultant, National Heart Institute, executive director, National Advisory Heart Council, and formerly clinical professor of medicine, Harvard Medical School, and physician, Massachusetts General Hospital.

4:30–5:15. **Preventive Measures in the Management of Heart Disease.** David Rutstein, professor of preventive medicine, Harvard Medical School.

5:15–5:30. **The Role of the New England Heart Association in Sponsoring Local Heart Programs.** Laurence B. Ellis, president, New England Heart Association, assistant clinical professor of medicine, Harvard Medical School, associate physician, Thorndike Memorial Laboratory, and assistant visiting physician, Boston City Hospital.

5:30–6:00. **The Diagnosis and Treatment of Angina Pectoris.** Joseph E. F. Riseman, associate in medicine, Harvard Medical School, and visiting physician, Beth Israel Hospital.

Monday, March 14. CARDIOVASCULAR DISEASE. Chairmen: Laurence B. Ellis and Eugene Eppinger.

7:00–7:45. **Curable Heart Disease.** C. Sidney Burwell, research professor of clinical medicine, Harvard Medical School, and physician, Peter Bent Brigham Hospital.

7:45–8:15. **The Use and Abuse of Laboratory Aids (Including Electrocardiography) in the Evaluation of Patients with Heart Disease.** Richard A. Bloomfield, instructor, Harvard Medical School, assistant physician, Thorndike Memorial Laboratory, and junior visiting physician, Boston City Hospital.

8:15–9:00. **The Diagnosis and Treatment of Rheumatic Fever — Its Complications.** Benedict F. Massell, clinical associate in pediatrics, Harvard Medical School, associate research director, House of the Good Samaritan, and chief, Rheumatic Fever Division, Children's Hospital.

Wednesday, March 16. INDUSTRIAL HEALTH AND ACCIDENTS. Chairmen: Henry C. Marble and Daniel L. Lynch.

4:00–4:20. **Industrial Health — Its Contributions and Opportunities.** Carl M. Peterson, secretary, Council on Industrial Health, American Medical Association.

4:20–4:40. **Injuries to the Hand.** Edward Hamlin, assistant surgeon, Massachusetts General Hospital.

4:40–5:00. **Industrial Diseases.** Albert O. Seeler, professor of industrial diseases, Harvard School of Public Health.

5:00–5:20. **Examination of Back Injuries.** Carroll Larson, assistant surgeon, Department of Orthopedics, Massachusetts General Hospital.

5:20–5:40. **Common Causes of Contact Dermatitis.** George E. Morris, consultant in Industrial Dermatology, Boston.

5:40–6:00. **Records and Reports in Industrial Accidents.** Henry C. Marble, consulting surgeon, Massachusetts General and Faulkner hospitals.

Monday, March 21. INFECTIOUS DISEASES. Chairmen: Chester S. Keefer and Louis Weinstein.

7:00–7:25. **Newer Antibiotic Agents — Polymyxin, Aureomycin and Chloromycetin.** Maxwell Finland, physician-in-chief, Fourth Medical Service, Boston City Hospital, and assistant professor of medicine, Harvard Medical School.

7:30–7:55. **Antibiotic Treatment of Pneumonia.** William Hewitt, instructor in medicine, Boston University School of Medicine, fellow, National Institute of Health, and staff member, Evans Memorial, Massachusetts Memorial Hospitals.

8:00–8:25. **The Treatment of Nephrosis by Induced Measles.** Charles A. Janeway, Thomas Morgan Rotch Professor of Pediatrics, Harvard Medical School, and physician-in-chief, Children's Hospital.

8:30–8:55. **Use of Chemotherapeutic Agents as Prophylaxis.** Benedict F. Massell, clinical associate in pediatrics, Harvard Medical School, associate research director, House of the Good Samaritan, and chief of the rheumatic fever division, Children's Hospital.

Wednesday, March 23. Medicolegal Problems. Chairmen: Alan R. Moritz and Richard Ford.

4:00–5:00. **The Doctor as Defendant and as Witness.** Richard Ford, associate medical examiner of Suffolk County, and member of teaching staff, Department of Legal Medicine, Harvard Medical School.

5:00–6:00. **Scientific Evidence in Criminal Investigation.** Russell Fisher, Rockefeller Fellow, Department of Legal Medicine, Harvard Medical School.

Monday, March 28. Headache. Chairmen: James L. Poppen and John B. Dynes.

7:00–7:45. **Headache Caused by Intracranial Neoplasms.** James L. Poppen, neurosurgeon, Lahey Clinic and New England Deaconess and New England Baptist hospitals.

7:45–8:25. **Migraine and Histamine Headache.** John B. Dynes, neuropsychiatrist, Lahey Clinic, and neurologist, New England Deaconess and New England Baptist hospitals.

8:25–9:00. **Headaches from a Psychiatric Standpoint.** Robert E. Arnot, research fellow in psychiatry, Harvard Medical School and Boston Psychopathic Hospital.

Wednesday, March 30. Gynecology. Chairman: Fred Simmons.

4:00–4:20. **Elementary Facts Concerning the Vaginal Smear.** Howard M. Ulfelder, assistant surgeon, Massachusetts General Hospital, and clinical associate in surgery, Harvard Medical School.

4:30–4:50. **Conservative Ovarian Surgery.** Samuel R. Meaker, professor of gynecology, Boston University Medical School.

5:00–5:20. **Conservative Management of Endometriosis.** John Fallon, director, Fallon Clinic, Worcester, Massachusetts.

5:30–6:00. **The Physiology of Menstruation (Animated Cartoon).** John Rock, clinical professor of gynecology, Harvard Medical School; and Somers H. Sturgis, assistant surgeon, Massachusetts General Hospital.

Monday, April 4. Obstetrics. Chairmen: M. Fletcher Eades and H. Bristol Nelson.

7:00–7:15. **X-Ray Pelvimetry and Its Clinical Interpretation.** Robert H. Barker, Boston Lying-in Hospital.

7:15–7:30. **Significance of Test of Labor.** Luke Gillespie, assistant in obstetrics and gynecology, Harvard Medical School, and assistant obstetrician, Boston Lying-in Hospital.

7:30–7:45. **Antibiotics in the Treatment of Uterine Sepsis.** Maxwell Finland, physician-in-chief, Fourth Medical Service, Boston City Hospital, and assistant professor of medicine, Harvard Medical School.

7:45–8:00. **Question Period.**

8:00–8:20. **Nonmenstrual Bleeding: Diagnosis and treatment.** John Rock, clinical professor of gynecology, Harvard Medical School.

8:20–8:40. **Treatment of Toxemia of Pregnancy.** Duncan Reid, Richardson Professor of Obstetrics, Harvard Medical School.

8:40–9:00. **Question Period.**

Wednesday, April 6. Gastroenterology. Chairmen: Francis D. Moore and Chester M. Jones.

4:00–4:20. **The Treatment of Bleeding Gastric and Duodenal Ulcer.** John E. Dunphy, senior associate in surgery, Peter Bent Brigham Hospital, and assistant professor of surgery, Harvard Medical School.

4:20–4:30. **Discussion.**

4:30–4:50. **The Value of Exfoliative Cytology in the Diagnosis of Gastric Carcinoma.** Howard M. Ulfelder, assistant surgeon, Massachusetts General Hospital, and clinical associate in surgery, Harvard Medical School.

4:50–5:00. **Discussion.**

5:00–5:20. **Nutritional Problems Arising from Anastomotic Surgery.** Chester M. Jones, physician, Massachusetts General Hospital, and clinical professor of medicine, Harvard Medical School.

5:20–5:30. **Discussion.**

5:30–5:50. **Body-Fluid Replacement in Gastrointestinal Surgery.** Francis D. Moore, surgeon-in-chief, Peter Bent Brigham Hospital, and Moseley Professor of Surgery, Harvard Medical School.

5:50–6:00. **Discussion.**

Monday, April 11. Hematology. Chairmen: Joseph F. Ross and Clement A. Finch.

7:00–7:20. **The Therapeutic Use of Folic Acid and Vitamin B_{12}.** William B. Castle, professor of medicine, Harvard Medical School, and director, Thorndike Memorial Laboratory and Second and Fourth Medical Services (Harvard), Boston City Hospital.

7:20–7:40. **Hemolytic Disorders: Practical applications of the Coombs test and other serologic technics.** Charles P. Emerson, Jr., assistant professor of medicine, Boston University School of Medicine, and visiting physician, Massachusetts Memorial Hospitals.

7:40–8:00. **The Clinical Use of Blood Fractions.** Charles A. Janeway, Thomas Morgan Rotch Professor of Pediatrics, Harvard Medical School, and physician-in-chief, Children's Hospital.

8:00–8:20. **Dicumarol and Heparin — Their Use and Abuse.** Clement A. Finch, associate in medicine, Harvard Medical School, and associate in medicine, Peter Bent Brigham Hospital.

8:20–8:40. **What Can be Accomplished in Treating Leukemia and Malignant Lymphoma.** Joseph F. Ross, associate professor of medicine, Boston University School of Medicine, and physician, Massachusetts Memorial Hospitals.

8:40–9:00. **Practical Management of the Rh Problem.** Louis K. Diamond, assistant professor of pediatrics, Harvard Medical School, physician and chief of Hematology Division and director of the Blood Bank, Children's Hospital.

Wednesday, April 13. Diseases of the Spinal Column. Chairmen: W. Jason Mixter and James C. White.

4:00–4:20. **Congenital Anomalies of the Spine and Spinal Cord.** Franc D. Ingraham, associate professor of surgery, Harvard Medical School, neurosurgeon-in-chief, Children's Hospital, and neurologic surgeon, Peter Bent Brigham Hospital.

4:25–4:45. **Neoplasm of the Spine and Cord.** James L. Poppen, neurosurgeon, Lahey Clinic and New England Deaconess and New England Baptist hospitals.

4:50–5:10. **Injuries of the Spine and Cord.** Donald Munro, associate professor of neurosurgery, Harvard Medical School and Boston University School of Medicine, and chief, Department of Neurosurgery, Boston City Hospital.

5:15–5:35. **Infectious Lesions of the Spine and Cord.** James C. White, associate professor of surgery, Harvard Medical School, and chief, Neurosurgical Service, Massachusetts General Hospital.

5:40–6:00. **Ruptured Intervertebral Disk.** W. Jason Mixter, member, Board of Consultation, Massachusetts General Hospital, and consultant on staffs of Beth Israel, Mt. Auburn and New England Deaconess hospitals.

Monday, April 18. PEDIATRICS. Chairmen: Warren R. Sisson and Charles A. Janeway.

4:00–5:00. **Allergy in Childhood.** Lewis Webb Hill, visiting physician and chief of Allergy Clinic, Children's Hospital, and clinical associate in pediatrics, Harvard Medical School.

5:00–6:00. **Question Period.**

Wednesday, April 20. PSYCHIATRY. Chairman: Harry C. Solomon.

4:00–5:00. **Office Practice in Psychiatry.** Donald J. MacPherson, instructor in medicine, Harvard Medical School, and associate in medicine, Peter Bent Brigham Hospital.

5:00–6:00. **The Psychoses and the Mental Hospital.** Walter E. Barton, superintendent, Boston State Hospital.

Monday, April 25. CLINICAL PROBLEMS IN INTERNAL MEDICINE (The Recognition of Some Rare but Often Curable Diseases Which Masquerade as Common Disorders). Chairmen: Samuel H. Proger and Lewis Dexter.

7:00–7:25. **Neurology.** Raymond D. Adams, assistant professor of neurology, Harvard Medical School, lecturer in neurology, Tufts College Medical School, and visiting neurologist and neuropathologist, Boston City Hospital.

7:30–7:55. **Hematology.** William Dameshek, professor of clinical medicine, Tufts College Medical School, and consultant in hematology and visiting physician, Joseph H. Pratt Diagnostic Hospital.

8:00–8:25. **Cardiology.** Samuel A. Levine, assistant professor of medicine, Harvard Medical School, and physician, Peter Bent Brigham Hospital.

8:30–8:55. **Endocrinology.** Elmer C. Bartels, physician, Department of Internal Medicine, Lahey Clinic, and physician, New England Baptist and New England Deaconess hospitals; Frank N. Allan, executive director, Department of Internal Medicine, Lahey Clinic, and physician, New England Baptist and New England Deaconess hospitals; and Lewis M. Hurxthal, head of Department of Internal Medicine, Lahey Clinic, and physician, New England Baptist and New England Deaconess hospitals.

Wednesday, April 27. FRACTURES. Chairman: Otto J. Hermann.

4:00–4:25. **Elbow Fractures and Epiphyseal Injuries of Childhood.** David S. Grice, associate orthopedic surgeon, Children's Hospital.

4:25–4:50. **Injuries to Foot and Ankle.** Joseph Shortell, surgeon-in-chief, Orthopedic Service, Boston City Hospital.

4:50–5:00. **Question Period.**

5:00–5:25. **Postoperative Care of Fractures of the Hip.** Edwin F. Cave, chief, Fracture Service, Massachusetts General Hospital.

5:25–5:50. **The Needs and Benefit of Medical Rehabilitation.** Augustus Thorndike, chief surgeon, Department of Hygiene, Harvard University.

5:50–6:00. **Question Period.**

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The March schedule for Consultation Clinics for Crippled Children in Massachusetts under the provisions of the Social Security Act follows:

CLINIC	DATE	CLINIC CONSULTANT
Haverhill	March 2	William T. Green
Lowell	March 4	Albert H. Brewster
Salem	March 7	Paul W. Hugenberger
Gardner	March 8	Carter R. Rowe
Brockton	March 10	George W. Van Gorder
Greenfield	March 14	Charles L. Sturdevant
Springfield	March 15	Garry deN. Hough, Jr.
Pittsfield	March 16	Frank A. Slowick
Worcester	March 18	John W. O'Meara
Hyannis	March 24	Paul L. Norton
Fall River	March 28	David S. Grice

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

MISCELLANY

AMERICAN CANCER SOCIETY

Dr. Clarence L. Scamman, director of the Division of Public Health of the Commonwealth Fund of New York from 1931 to July 15, 1948, has returned to Boston as medical director of the Massachusetts Division of the American Cancer Society.

Prior to 1931 Dr. Scamman was deputy commissioner of public health of the Commonwealth of Massachusetts.

BUSINESS MANAGER OF HARVARD UNIVERSITY MEDICAL AREA

Mr. Charles W. Greenough, formerly Budget Commissioner of the Commonwealth of Massachusetts, has been appointed business manager for the Medical Area of Harvard University. He will assist the deans with budget and business affairs of the Medical School, the School of Dental Medicine and the School of Public Health.

YOUR LEGISLATORS

want to know your opinion on matters vital to you.

The Committee on Legislation of the Massachusetts Medical Society is preparing a booklet listing state legislators according to district societies. If you wish a copy, please apply to Society Headquarters, 8 Fenway, Boston 15.

Name .....

Address .....

Number of copies .....

CORRESPONDENCE

ASSURANCE NEEDED

To the Editor: Enclosed is a copy of a letter sent to the Secretary of the American Medical Association and signed by fifteen Springfield physicians, which is forwarded for publication in your columns in case you consider it of sufficient interest.

HOWARD N. SIMPSON, M.D.

Springfield, Massachusetts

George F. Lull, M.D.
Secretary and General Manager
American Medical Association
535 North Dearborn St.
Chicago 10, Ill.

Dear Dr. Lull:

The undersigned physicians, members of the American Medical Association, have received your letter and the enclosed literature regarding the $25.00 assessment voted by the House of Delegates, which you choose to describe as "the democratically chosen body that speaks for the American Medical Association." The dictionary definition of "democratic" is "chosen by the people" which the House of Delegates is not and can not be according to the Association's by-laws. We have no desire, at the present time, to make an issue of this, but merely wish to point out that these delegates, whom we did not elect, have seen fit to demand our support and our money, but have evinced no interest whatsoever in our opinions as to whether the assessment was justifiable or how it was to be spent. Because we believe that quarreling and disunity among ourselves at this time would be disastrous we shall pay the assessment provided we may have assurances, either privately or through the press, that our money will be used in a more enlightened manner than your letter implies.

Let us make it clear at this point that the undersigned are physicians deriving all, or nearly all, their income from private practice. We believe in private practice; we believe in the high standards of American medicine, and we view with profound concern the impending threat to these standards inherent in any universal method of government financing and control of medicine.

We also believe that the fundamental issues are becoming beclouded in the barrages and counter-barrages detonated by Mr. Ewing on one side and Dr. Fishbein on the other. We believe no useful purpose is served by hurling insults and ridicule either at public officials or at private doctors.

We believe that the American Medical Association, with its all-too-recent embrace of the Blue Cross and Blue Shield plans, is at a very definite disadvantage in the public mind.

We believe that there is at the present time in this country a very definite political trend to the left. Whether we like it or not we must face the facts and deal with them. We hold it to be highly questionable whether a group such as the presently constituted House of Delegates is capable of successfully challenging such a political trend.

We believe that the course of action outlined in your letter will lead only to defeat. The public is tired of sneers, of clichés, and of propaganda. A large segment of the public — the voting public — believes that the cost of medical care is too high. They realize that the medical profession in America has made great advances in science, but has contributed almost nothing to the solution of the economic problems of the ill.

We believe that organized medicine needs leadership and an enlightened attitude toward modern problems; that our duty to our patients and to ourselves is not to fight blindly against the administration and the trend of history, but rather to formulate a specific legislative program which is positive, forward-looking, practical, and humanitarian. There are portions of the Ewing program, such as extension of public health services and improved distribution of trained manpower, which the vast majority of the profession would be willing to accept; there are changes in the present medical economic set-up which the public demands. We believe that by substituting harmony for hatred, and co-operation for conflict many of our problems may be resolved.

Finally, we believe that we are better trained and equipped to consult than to fight. We believe that the 81st Congress would be more favorably influenced by the subtler suasions of the bedside manner than by the outpourings of a California propaganda mill.

Changes will be made, and in these changes it is far better that we lead than that we be driven. There is no other way that American medicine can maintain its prestige in the world, or that we, as individuals can practice our profession with dignity and with honor.

Very sincerely yours,

HOWARD N. SIMPSON, M.D.
RAYMOND L. BARRETT, M.D.
WILLIAM J. DEVLIN, M.D.
FRANK J. JORDAN, JR., M.D.
EDWARD J. FERRARONE, M.D.
BARRON D. KNOX, M.D.
HORACE B. PEASE, M.D.
CHARLES C. DERRICK, M.D.
HARRY L. ROBERTS, M.D.
W. O. WILDER, M.D.
JAMES L. SMEAD, M.D.
ALLEN S. JOHNSON, M.D.
WAYNE C. BARNES, M.D.
FREDERICK D. JONES, M.D.
THEODORE R. MINER, M.D.

NOTE: Delegates to the American Medical Association are elected by the council of the state society. The councilors are the representatives of their district society. — ED.

NOTICES

ANNOUNCEMENTS

Dr. Frank P. Cahill announces the opening of his office for the practice of general surgery at 395 Commonwealth Avenue, Boston.

Dr. Thomas E. Caulfield announces the opening of an office at 520 Commonwealth Avenue, Boston, for the practice of psychiatry.

Dr. Francis R. Kenney announces the opening of an office for the practice of general surgery at 319 Longwood Avenue, Boston.

Dr. C. Purcell Roberts announces the removal of his office from 26 Linden Avenue, N.E., to 762 Cypress Street, N.E., Atlanta, Georgia.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, March 3, at 7:15 p.m., in the classroom of the Nurses' Residence. Dr. Marianne Taylor will speak on the subject "Gynecologic Conditions Viewed from the Psychosomatic Angle." Dr. Lucile Lord-Heinstein will be chairman.

AMERICAN ACADEMY OF PEDIATRICS

Publication of the national report on the findings of the recently completed two-and-a-half-year study of child health services will be marked by a dinner on April 2 in New York City, according to an announcement of Dr. Warren R. Sisson, president of the American Academy of Pediatrics. A nationally known layman and an outstanding authority in medicine and public health are being invited to be guest speakers. The two-volume report, which is now in press, is being published by the Commonwealth Fund of New York.

(*Notices concluded on page xiii*)